Objectives: Oral cancer etiology is multifactorial and the main risk factors are tobacco chewing and smoking along with alcohol consumption and viruses. In the current study from a South Indian population, we sought to determine the role of HPV 16 in the pathogenesis, its concordance with p16 over expression in OSCC. Preliminary examination on FFPE embedded OSCC (n = 297) sample was observed by H & E staining, and cases showing cytological changes were selected.

Findings: HPV 16 DNA prevalence were assessed by Conventional PCR method which showed 128 out of 297 samples positive for HPV16 DNA. Further, the frequency distribution of HPV 16 E6/E7 in 128 tissues was evaluated by qPCR which showed 97 samples were positive for HPV16 E6 qPCR and 98 samples positive for HPV16 E7 qPCR. For the same 128 samples immunohistochemistry was conducted for p16 evaluation.Out of 128 tissue samples, 19 tissue samples were found to be positive for p16 overexpression (+++). Evaluation of mRNA expression of E6 and E7 in the 19 samples was estimated by flow-cytometry, which revealed only 7 samples positive for the mRNA expression. There was no correlation between p16 expressed (+++) samples and quantification of HPV16 mRNA expressions. From these investigations the role of HPV in the etiology, pathogenesis of OSCC was not established.

Conclusion: This led to the performance of meta-analysis in which studies pertaining to HPV-related OSCC evaluated by application of conventional and qPCR, flow cytometry and IHC for the detection of DNA, mRNA and p16 overexpression, respectively were included. The results obtained were indicative that HPV prevalence in the oral cavity is low and unlikely to play a major significant or decisive role in the etiology, pathogenesis of OSCC. Our results were in accordance with the meta analysis results.

WNT/B-CATENIN SIGNALING PATHWAY REGULATES TUMOR-INITIATING CELLS IN HEAD AND NECK SQUAMOUS CELL CARCINOMA.

DR. CHIA-CHENG LI[A], DR. CHENG-CHIA YU[B], DR. RESHMA MENON[C], MS. INGRID CARVO[A], DR. ZHE LI[D]. [A] HARVARD SCHOOL OF DENTAL MEDICINE, [B] SCHOOL OF DENTISTRY, CHUNG SHAN MEDICAL UNIVERSITY, [C] N/A, [D] DEPARTMENT OF MEDICINE, DIVISION OF GENETICS, BRIGHAM AND WOMEN'S HOSPITAL

Objectives: Head and neck squamous cell carcinoma (HNSCC) is one of the leading cancers, with a 40% 5-year survival rate in advanced cases. HNSCC is notorious for its high recurrence rate and frequent occurrence of synchronous/metachronous primary tumors. Tumor initiating cells (TICs) model was proposed to explain its tumor heterogeneity and frequent recurrences. Lineage tracing is a genetic approach that allows identification of TICs in their native habitats and characterization of their in vivo behavior.

Findings: Our re-analysis of TCGA data revealed that high expression of AXIN2, a downstream target of Wnt signaling, was significantly correlated with low survival rate of HNSCC. To characterize the Wnt-responsive cell population, we established a carcinogen-induced model using Axin2-CreER reporter mice. After tamoxifen induction, clonal expansion of fluorescent reporter-positive cells (Wnt-responsive tumor cells) was visualized in the basal cell layer of epithelial dysplasia and HNSCC, suggesting the critical role of Wnt in regulating TICs in early stages of carcinogenesis. β-catenin and LEF1 immunofluorescent staining were performed to confirm Wnt activation. Lineage tracing was also accomplished in 3D organoid culture. The fluorescent reporter-positive cells were capable of forming organoids. Furthermore, application of cisplatin enriched AIXN2 cell population.

Conclusions: Activation of Wnt/β-catenin signaling pathway is an early event in HNSCC carcinogenesis. Lineage tracing using the Axin2-CreER reporter may link TICs properties with a fundamental signaling pathway in normal development. Further research is required to clarify the role of Wnt-responsive TICs in recurrence and therapy resistance of HNSCC.

ADENOID AMELOBLASTOMA: A SERIES OF 5 TUMORS.

DR. ELIZABETH ANN BILODEAU, DR. RAJA SEETHALA. UNIVERSITY OF PITTSBURGH

Background: First described in 1959 by Waldron and more fully characterized by Loyola et. al. in 2014, adenoid ameloblastoma (with dentinoid) is a rare odontogenic tumor variant with less than 20 reported cases in the literature.

Objectives: Adenoid ameloblastomas were identified after review of ameloblastomas from the University of Pittsburgh Medical Center Department of Pathology archives from 1990 to 2018.

Findings: A review of our archives yielded 6 cases of adenoid ameloblastoma in 5 patients. Of these, 2 tumors were obtained from the "in-house" pathology files with one tumor being a recurrent adenoid ameloblastoma, whereas the remaining were consultations. The 4 cases (in 3 patients) received in consultation had a differential diagnosis of a salivary neoplasm. All cases were in the maxilla (5/5, 100%), 60% were in males, with a mean age of 52.6 years (range 29-65), and mean size of 5.8 cm (range 4.0 to 7.8 cm). Increased mitotic activity was present in all cases, (mean 7 mitoses/10hpf, range 3-11 mitoses/10hpf). All tumors exhibited pseudoglandular spaces. Other common histologic features included whorls or morules, clear cells, ghost cells, and matrix production with hard tissue formation. Immunohistochemically, the tumors were positive for p63 (3/3, 100%), beta catenin within the morules (2/3, 66.6%), AE1/3 (1/1, 100%), CK5/6 (1/1, 100%), vimentin (1/1, 100%), CEA (2/2, 100%), p40 (1/1, 100%) and negative for BRAF V600E (0/3, 0%), calretinin (0/2, 0%), CK7 (0/1, 0%), SMA (0/4, 0%), S100 (0/3, 0%), Sox-10 (0/1, 0%), TTF-1(0/1, 0%), Pax-8 (0/1, 0%), p16 (0/1, 0%).

Conclusions: Adenoid ameloblastoma (with dentinoid) is a rare, aggressive odontogenic tumor variant with morphologic overlap with salivary neoplasms. Given the histologic similarities to other tumors and the high rate of recurrence, further characterization of this entity is needed

PRIMARY INTRAOSSEOUS SOFT TISSUE MYOEPITHELIOMA OF THE MANDIBLE: CASE REPORT AND LITERATURE REVIEW.

DR. LAMA ALABDULAALY, DR. SOOK BIN WOO. HARVARD SCHOOL OF DENTAL MEDICINE

Introduction: Soft tissue myoepithelioma (STM) is a benign tumor composed of spindled and epithelioid cells arranged in various patterns within chondromyxoid stroma. While salivary gland myoepithelioma has been well-recognized as a variant of pleomorphic adenoma, the absence of normal myoepithelial cells within STM may be why STM was only recently-recognized. The occurrence of STM within the bone is

rare with only 16 cases reported in the literature, none of which have been reported in the mandible.

Case Report: A 14-year-old female presented with a lobulated gingival nodule measuring 1.2 × 0.8 cm between teeth #20 and 21. Radiographically, the lesion was a well-circumscribed, non-corticated multilocular radiolucency between the roots of #20 and #21 measuring 1.4 × 1.0. cm, extending from the alveolar crest to close to the root apices. An incisional biopsy was performed. Microscopically, the lesion consisted of a non-encapsulated, multilobular tumor composed of a proliferation of spindle and epithelioid cells within a delicate myxochondroid stroma. Tumor cells were positive for S-100, vimentin, neuron-specific enolase (NSE) and epithelial membrane antigen (EMA) and negative for CAM5.2, AE1/3, SMA, SOX-10, CD57, glial fibrillary acidic protein (GFAP), and p63. Ki-67 labeled less than 5% of the cells. These findings are suggestive of STM, and the bone and soft tissue consultant pathologist concurred with this diagnosis.

Discussion: The putative cell of origin for this tumor is a stem cell within the soft tissues that differentiates towards a cell with myoepithelial phenotype. Unlike salivary gland myoepithelioma which harbors PLAG1 and HMGA2rearrangements, STM harbors the EWSR1 rearrangement in up to 44% of the cases. Ectomesenchymal chondromyxoid tumor may represent the same entity since it has similar histomorphology and immunohistochemical profile but exhibits EWSR1 rearrangement in only 25% of cases. To our knowledge, this is the first report of a STM occurring in the mandible.

PROGNOSTIC CLASSIFIER FOR ORAL POTENTIALLY MALIGNANT DISORDERS: AN INTEGRATED HISTOPATHOLOGICAL AND MOLECULAR APPROACH.

DR. HANS PRAKASH SATHASIVAM, PROF. PHILIP SLOAN, DR. RALF KIST, DR. MAX ROBINSON. NEWCASTLE UNIVERSITY

Objectives: Oral squamous cell carcinoma (OSCC) is associated with a high degree of morbidity and mortality. OSCCs are often preceded by oral potentially malignant disorders (OPMD) which have a higher propensity to undergo malignant transformation (MT) compared to clinically normal oral mucosa. Currently there is no reliable method to determine which OPMD cases will undergo MT. This study was performed to construct a prognostic classifier for patients with OPMD by integrating clinical, histopathological and molecular factors and to discover a gene expression signature that characterises OPMD with a high risk of undergoing MT.

Findings: Statistical analysis of an OPMD patient cohort (23 MT vs. 25 with no MT) showed that site of initial OPMD ($p = 0.043$), binary oral epithelial dysplasia (OED) grading ($p = 0.009$) and loss of heterozygosity at 3p/9p/17p ($p = 0.026$) were statistically significant. Other demographic factors, clinical features and the WHO 3-tiered OED grading system were not statistically significant. Gene expression experiments revealed several genes that were differentially expressed between OPMD that underwent MT and those that did not [false discovery rate of < 0.05]. Statistical model building was performed, and the outputs were used to construct a prognostic classifier.

Conclusions: Our findings show that a classifier combining histopathological and molecular factors outperforms conventional methods for prognosticating clinical outcome in patients with OPMD. We have also shown that formalin-fixed paraffin-embedded tissue can be used to generate a molecular classification with clinical utility.

SOMATIC DRIVER MUTATIONS IN ORAL AND SINONASAL MUCOSAL MELANOMA. A REFERRAL CENTRE EXPERIENCE IN MEXICO CITY.

DR. JESSICA LISSETE MALDONADO MENDOZA[A], DR. VELIA RAMIREZ-AMADOR[A], DR. GABRIELA ANAYA SAAVEDRA[A], DR. ERIKA RUÍZ GARCÍA[B], DR. HÉCTOR MALDONADO MARTÍNEZ[B], DR. EDITH FERNÁNDEZ FIGUEROA[F], DR. ABELARDO MENESES GARCÍA[B]. [A] UNIVERSIDAD AUTÓNOMA METROPOLITANA XOCHIMILCO, [B] NATIONAL CANCER INSTITUTE OF MEXICO, [F] COMPUTATIONAL GENOMICS, NATIONAL INSTITUTE OF GENOMIC MEDICINE

Objective: Oral and sinonasal mucosal melanomas (OSNMM) are aggressive tumors with low survival and few therapeutic alternatives. The aim of this study was to describe the prevalence of mutations in NRASQ61K, BRAFV600E, CKITL576P, K642E, MITFE318K and PTENR130;and to analyze the clinic-pathological features present.

Findings: Cross-sectional and observational study that included cases with OSNMM from the National Cancer Institute of Mexico City and the Oral Pathology Laboratory of UAM-X (January 2000-December 2016). Demographic and clinical data were obtained, and histopathological diagnosis was confirmed. Genomic DNA was obtained and molecular analysis was carried out through quantitative polymerase chain reactions (qPCR) (Customized Biomarker somatic mutation Array®, Qiagen). The statistical analysis was performed using the SPSS v20 software.

Forty-eight cases were included, 56.2% were sinonasal melanomas (SNM) and 43.7% oral melanomas (OM). The median age of the individuals was 60 years (Q1-Q3 = 51-74), 54.2% of the cases were men. Higher symptomatology percentages were found among SNM (100% vs. 52.9%, $p<0.001$). At the histopathological analysis, 97% of the tumors showed vertical and infiltrative growth, SNM showed a greater amount of necrosis (68% vs. 32%, $p= 0.006$) in comparison with OM. Eight (16.6%) OSNMM presented at least one mutation: 6/28 (21.4%) SNM cases and 2/20 (10%) OM. From 48 OSNMM, three (6.6%) showed V600E BRAFmutation, 3/48 (6.2%) Q61R mutation NRAS and 2/48 (4.1%) K624E mutation KIT. No mutations were found in MITF or PTEN.

Conclusions: A low prevalence of mutations was found. Somatic driver mutations might not be related with OSNMM development; thus, the current biological agents (vemurafenib and imatinib) may probably be ineffective against OSNMM. It is necessary to continue the search of other molecular alterations to suggest therapeutic alternatives for these tumors, such as: proteins amplification (c-KIT) or epigenetic mechanism which might regulate the genetic expression (miRNAs).

APPLICATION OF DEEP LEARNING ALGORITHMS IN DETECTION OF MITOTIC EVENTS IN ORAL SQUAMOUS CELL CARCINOMA USING CELLPHONE IMAGES.

DR. AMBER KIYANI[A], DR. HASSAN AQEEL[B], MR. ASJID TANVEER[B], MR. WAJAHAT NAWAZ[B], DR. SYED ALI KHURRAM[C]. [A] RIPHAH INTERNATIONAL UNIVERSITY, [B] NATIONAL UNIVERSITY OF SCIENCE AND TECHNOLOGY, [C] UNIVERSITY OF SHEFFIELD