Immunohistochemical expression of pan-Trk in a large cohort of salivary gland neoplasms: preliminary results.

Monday, 27th April - 08:30: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 69

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Introduction: Neurotrophic tyrosine receptor kinases (NTRK) represent a group of proteins that actively partici- pate in cell survival, proliferation, and differentiation processes. NTRK gene rearrangements have been identified in several neoplasms, including secretory carcinoma of the salivary glands (ETV6-NTRK3). A newly developed pan-Trk antibody for immunohistochemistry (IHC) was able to identify and differentiate cases of secretory carcinoma from mimics by its nuclear staining. However, different patterns of expression (cytoplasmic and/or membranous) have also been reported in benign and malignant salivary gland neoplasms (SGN). Due to this apparent heterogeneous staining profile, the significance of pan-Trk IHC in SGN is still unclear. **Materials and Methods:**Cases of salivary mucoepidermoid carcinoma (MEC), polymorphous adenocarcinoma (PAC), adenoid cystic carcinoma (AdCC), acinic cell carcinoma (ACC), epithelial-myoepithelial carcinoma (EMC), and secretory carcinoma (SC) were retrieved between 2003 and 2019 from the University of Iowa, College of Dentistry archives. Pan-Trk IHC was performed in tissue microarrays. IHC pattern of expression and intensity (H-score) were assessed. **Results:**Patient cohort was comprised of 41 women and 20 men with a median age of 61 years old. The most common location was the palate followed by the buccal mucosa. Pan-Trk is positive predominantly in the nucleus of SC (H-score=23.6), and in the cytoplasm/membrane of PAC (H-score=12.2), MEC (H-score=5.6), AdCC (H-score=13.5), and EMC (H-score=21.4). However, nuclear staining was also present in a small subset of PAC, MEC, and AdCCs. Notably, Pan-Trk was negative in all ACC samples. **Conclusions:**Preliminary data suggests that pan-Trk nuclear staining is not exclusive to SC. Furthermore, the cytoplasmic/membranous pattern seen in non-SC neoplasms may indicate the presence of NTRK gene rearrangement. A better understanding about the pan-Trk staining pattern could not only improve its diagnostic value, but also contribute identifying patients that would benefit from targeted-therapies using NTRK inhibitors (*e.g.* entrectinib, larotrectinib).

Decreased expression of ATF-3 in melanoma promotes tumor growth via ERK and AKT pathways

Monday, 27th April - 08:42: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 64

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Introduction: Activating transcription factor 3 (ATF-3), a cyclic AMP-dependent transcription factor that is encoded by the ATF-3 gene, plays a regulatory role in melanoma, although its function during tumor progression is unknown. Here we evaluated ATF-3 expression during melanoma evolution to elucidate its role in melanogenesis.

Materials & Methods: Primary and metastatic melanoma cell lines, patient melanomas and murine melanoma xenografts were evaluated by immunofluorescence, Western Blot and RT-PCR studies. Melanoma cell lines were retrovirally transfected with ATF-3 overexpressing vectors and CCK8, wound healing and Matrigel invasion studies were performed to test for proliferation, migration and invasive properties, respectively. Xenograft murine models were designed by subcutaneously injecting melanoma cells or its overexpressed counterpart into the anterior and posterior flanks of nude mice to evaluate tumor size and rate of formation.

Results: By immunofluorescence, ATF-3 staining declined in metastatic versus primary melanoma cell lines and with progression from patient nevi to primary to metastatic melanomas. Analysis of TCGA skin cutaneous melanoma database showed that lower ATF-3 expression correlated with poor prognosis. Metastatic melanoma cell lines with retrovirally-induced ATF-3 overexpression (A2058 and C8161 ATF-3 OE) exhibited decreased prolif- eration, migration and invasion. GO and KEGG analyses of our RNA seq data showed downregulation of phospho- rylated ERK and AKT in A2058 ATF-3 OE cells that was further validated by Western Blot. In vivo, xenografted A2058 ATF-3 OE cells formed smaller and less abundant tumors in murine subcutis than did control cells, and Ki-67 staining confirmed lower labeling indices in ATF-3 overexpressing lesions.

Conclusions:ATF-3 expression is associated with melanoma virulence and thus provides a potential target for novel therapies and predictive biomarker applications.

Regulatory Mechanisms of Endogenous APOBEC3B Expression in HPV(+) and (–) Oral Premalignancies and Head and Neck Cancer

Monday, 27th April - 08:54: Oral Essay Programs - Oral (Regular) - Abstract ID: 65

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Introduction:HPV(+) oral and oropharyngeal squamous cell carcinoma (OOPSCC) shows strong association with high-risk HPV16 and 18. The DNA cytosine deaminase APOBEC3B constitutes a major endogenous source of muta- tions in a wide variety of cancers. APOBEC3B causes C-to-T/-G base substitutions in 5′-TCA/T trinucleotide motifs and is overexpressed in head and neck cancer (HNC). High-risk HPV infection and dysregulation of the RB/E2F axis regulate *APOBEC3B in vitro*. Here, we investigate changes of APOBEC3B levels in HPV(+) and (–) oral epithelial dysplasia (OED) and OOPSCC, and probe whether APOBEC3B upregulation correlates with cellular proliferation.

Materials and Methods:APOBEC3B and Ki67 expression was assessed by immunohistochemistry in HPV(+) OED (n=10) and OOPSCC (n=28), and HPV(–) low-grade (n=42) and high-grade OED (n=38), and OSCC (n=46). Epithelial hyperplasia (OEH, n=14) and normal adjacent epithelium (n=10) served as controls. APOBEC3B H-scores and percentage of Ki67(+) cells were calculated using the Aperio ScanScope XT platform. Public NGS datasets available through TCGA were mined to identify molecular mechanisms associated with APOBEC3B upregulation in HNC.

Results: High-risk HPV significantly upregulated APOBEC3B in OED (Kruskal-Wallis test, $p<0.05$) and OOPSCC ($p<0.01$) compared to OEH. HPV(+) OEDs and tumors showed strong and diffuse, nuclear APOBEC3B immunoreactivity which mirrored p16 staining and coincided with disrupted p53 expression. Progressive APOBEC3B upregulation was observed in HPV(–) lesions; high-grade premalignancies and OSCCs showed significantly elevated APOBEC3B H-scores compared to low-grade OED ($p<0.01$) and controls ($p<0.01$). High mRNA and protein APOBEC3B levels strongly associated with advanced histologic grading in HPV(–) OSCC ($p<0.01$). A positive linear correlation was evident between APOBEC3B and Ki67 expression (Pearson's $r=0.5$), while RNAseq analysis suggests cell cycle regulation of APOBEC3B in HPV(–) HNC.

Conclusions: High-risk HPV drives upregulation of APOBEC3B in viral-related OED and HNC. In non-viral lesions, APOBEC3B levels also increase in a mechanism associated in part with cellular proliferation.

Retrospective Series of Burning Mouth Syndrome Patients Treated with a Protective Mouthguard: An Effective Non-Pharmacologic Treatment Modality

Monday, 27th April - 09:06: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 35

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Background: Burning mouth syndrome (BMS) is a relatively common condition defined as a relentless, idiopathic burning sensation of the oral mucosa after exclusion of other underlying causes of burning. Currently effective treatment is limited mostly to pharmacologic interventions. The use of non-pharmacologic therapy, specifically the use of protective mouthguards has not been well studied. This study evaluates effectiveness of mouthguards in patients treated for BMS at University of Florida College of Dentistry (UFCD). **Material and Methods**: Following IRB approval, the clinical database was retrospectively searched for patients diagnosed with BMS and treated with mouthguard between 2014-2019. Inclusion criteria included a minimum of 6-month follow-up and patients were excluded if treatment records were incomplete. Demographics, clinical data, medical history, and other treatment modalities were recorded and analyzed. **Results**: A total of 16 cases were included and a mean age of 67 years (range of 50-82) and a female: male ratio of 4.3:1 was identified. The average duration of burning symptoms prior to the first visit was 43 months. The location of symptoms involved tongue only (n=11, 69%); tongue, palate, and lips (n=2, 12.5%); tongue and palate (n=2, 12.5%); and tongue and lips (n=1, 6%). The most common concurrent medical conditions were hypothyroidism (n=7, 43.7%), hypertension (n=6, 37.5%), and diabetes (n=3, 18.7%). Study patients took a median of 6.5 concurrent medications. Six patients (37.5%) had symptomatic relief with mouthguard ther- apy in conjunction to concurrent standard BMS pharmacologic therapy, 37.5% of patients (n=6) had symptomatic relief with the mouthguard alone, and 25% of patients (n=4) reported no relief from the mouthguard. **Conclusion**: In this study a total of 75% of BMS patients reported improvement of subjective symptoms with the use of a pro- tective mouthguard, demonstrating the potential effectiveness of mouthguard as a non-pharmacologic therapeutic modality for BMS patients.

Case series of Adenomatoid Odontogenic Tumors: Clinical, Radiographic, and Histologic Features

Monday, 27th April - 09:18: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 40

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OBJECTIVE: We present a case series of adenomatoid odontogenic tumor (AOT), a benign odontogenic tumor from a large biopsy service. AOT has a limited growth potential and is often seen in children and young adults, between the ages of 10-19 years. AOT has uncertain pathogenesis and studies suggest enamel organ, reduced enamel epithelium, and rests of Malassez as potential sources. Clinically, AOT's are asymptomatic and identified upon routine radiographic examination. METHODS: Information was collected from the University of Florida Oral Pathology Biopsy Service archives (1994-2019). The clinical and demographic data along with any accompanying radiographic images and original slides were evaluated. RESULTS: A total of 26 cases of AOT were identified, with a mean age of 22.3 years (range: 12-67). A slight female predilection was noted (57.7%, n=15). Most cases presented in the anterior region of the jaw (73%, n=19) and a slight maxillary predilection was observed (61.5%, 16 cases). Most patients were aged under 20 (69.2%, n=18). Clinical impression included dentigerous cyst, lateral periodontal cyst, and odontogenic keratocyst (57.7%, n=15). Radiographs were available for six cases and all presented as a unilocular radiolucency. The histologic diagnosis was consistent with AOT in 24 cases and peripheral AOT in two cases.One case had a fo- cal area of CEOT that tested positive with a Congo Red stain. CONCLUSION: In almost all cases within the study the clinical impression of AOT was not rendered. This implied that AOT is rarely considered in the differential of such lesions. In addition, while most patients were children or young adults, there were a few outliers above thirty (19.2%, n=5). This may suggest that AOT is diagnosed late in some cases due to its benign nature. Clinicians should be sentient of this lesion as the treatment and prognosis differs from other odontogenic cysts and tumors.

Epithelial-Mesenchymal Transition Marker Brachyury Is Not Expressed in Spindle Cell Carcinoma of the Head & Neck

Monday, 27th April - 09:30: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 11

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Introduction. Epithelial-mesenchymal transition (EMT) is a complex biologic process by which epithelial cells lose their cytomorphologic characteristics and assume the phenotype of mesenchymal cells. EMT is essential to normal human embryogenesis, and also occurs in wound healing, tissue repair and cancer progression. Acquisition of a mesenchymal phenotype via EMT enhances the migratory capacity of carcinoma cells, increasing their metastatic capability and worsening prognosis for patients. One emerging marker of EMT is brachyury, a T-box transcription factor protein. Recent studies have demonstrated upregulation of brachyury in several carcinoma types, including squamous cell carcinoma (SCC). Spindle cell carcinoma (SpCC) is a variant of SCC in which cancer cells have a predominantly spindled phenotype. Whether brachyury is expressed in SpCC and contributes to this phenotypic change is not clear. **Objective.**To examine brachyury expression by immunohistochemistry in SpCC of the head & neck, hypothesizing that brachyury expression is increased in SpCC, as compared with other forms of SCC. **Methods.**Immunohistochemical staining for brachyury was performed on 20 head and neck carcinoma cases per group in each of four groups: SpCC; moderately- to well-differentiated SCC; moderately- to poorly-differentiated SCC; and verrucous carcinoma (VC). Uninflamed fibroma was the negative control; and human chordoma, along with a 14.5-day-old mouse embryo, were positive controls. Evaluation of brachyury reactivity was completed by light microscopy. **Results.**Brachyury expression was not seen in any of the experimental groups. Nuclear reactivity was present in both positive controls, including within chordoma cells, and within the nucleus pulposus of the mouse embryo. **Conclusions.**Brachyury does not appear to be involved in the cytomorphologic changes present in SpCC, nor is it expressed in any head & neck SCC variants. Our results are contrary to those found in previous reports. This result supports the hypothesis that an alternate mechanism contributes to the phenotype of SpCC.

Autocrine Signaling of Neuropilin 1 Receptor Promotes Tumor Growth in Oral Squamous Cell Carcinoma

Monday, 27th April - 09:42: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 27

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Introduction: Tumor angiogenesis is one of the hallmarks of oral squamous cell carcinoma (OSCC). Neuropilin 1 (NRP1) is a transmembrane receptor that binds angiogenic factors in the VEGF family in complex with VEGF receptor tyrosine kinases (RTKs) to stimulate the sprouting of blood vessels during neovascularization. Previously, our laboratory published that NRP1 is restricted to the suprabasal epithelium in normal oral mucosa, but is upregulated in the basal cell layer in dysplastic lesions. In OSCC, NRP1 expression was correlated with VEGF levels and tumor angiogenesis. NRP1 is not a kinase, therefore its role in epithelial or carcinoma cells which typically lack VEGF RTKs is unknown. Our aim is to determine the role that Nrp1 plays in OSCC tumorigenesis and explore the mechanistic action of NRP1 in carcinoma cells. **Methods/Results:** To characterize the role of Nrp1 in keratinocytes during tu- morigenesis, K14-Cre^{ERT};Nrp1-floxed (Nrp1-iKO) mice were treated with 4-Hydroxytamoxifen to induce Cre activity to delete the *Nrp1* gene. Deletion in the epithelial compartment was confirmed using Nrp1 immunostaining on biop- sied tissues. Nrp1-iKO and control (K14-Cre) mice were given 4-NQO carcinogen in the drinking water, ad libitum, for 16 weeks to generate premalignant lesions and OSCC, then moved to regular drinking water for 9 weeks and then euthanized and necropsied. Results indicated fewer tumor incidence and smaller tumor size in the Nrp1-iKO group than in the control group. *In vitro* data confirmed a direct effect of VEGF on the growth of the human OSCC cell line (HSC3) in colony formation in soft agar, while silencing of NRP1 inhibited colony growth compared to con- trols. **Conclusion:**Our data highlight the important role that NRP1 plays in OSCC and suggests that NRP1 signals in an autocrine fashion to enhance tumor growth in carcinoma cells.

The role of ANP32B as a biomarker and therapeutic target in head and neck cancer

Monday, 27th April - 09:54: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 37

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Introduction:
Acidic leucine-rich nuclear phosphoprotein 32 family member B (ANP32B) is involved in gene expression, apoptosis, cell proliferation, and cell cycle progression. The role of this protein in head and neck squamous cell carcinoma (HNSCC) pathogenesis is not yet known.
Materials and methods:
Biopsy specimens were analyzed from patients with HNSCC, oral cavity dysplasia, and benign tumors using miRNA TaqMan assays and quantitative polymerase chain reaction (n=45). Additionally, a luciferace reporter assay, loss of function and gain of function studies, and The Cancer Genome Atlas (TCGA) were used to perform analyses of gene expression data in relation with clinical data and survival outcomes.
Results:
micro-RNA analysis of patients with HNSCC and controls showed an increase in miRNA1-2 expression in patients with oral cancer ($P<0.05$). A luciferase reporter assay showed the role of miRNA 1-2 in the post translational regula- tion of ANP32B expression. Loss of function and gain of function studies showed a mechanistic role of the miRNA 1-2-ANP32B axis in carcinogenesis and AKT phosphorylation in HNSCC cell lines. Analysis of the Cancer Genome Atlas (TCGA) data showed a significant increase of ANP32B expression in head and neck cancer patients ($P<0.05$). Levels of ANP32B expression were significantly higher in stage 2-4 compared to stage 1 of HNSCC. Males with head and neck cancer showed a significantly higher expression of ANP32B compared to females ($P<0.05$). No differential expression of ANP32B between different races was found. ANP32B expression was significantly associated with a higher grade of tumor (P-trend<0.05). Higher expression of ANP32B was found in N3 and N2 metastasis stages versus N1. High expression of ANP32B in females was associated with the poorest prognosis ($P<0.05$).
Conclusions:
Altogether, our findings suggest that ANP32B acts as an oncogene in HNSCC and can be used as a potential thera- peutic target for HNSCC treatment.

Biodegradable Polylactide-co-Glycolide-Chitosan Janus Nanoparticles (JNP) for the Local Delivery of the IL-6R Receptor Antagonist, Tocilizumab, for Oral Squamous Cell Carcinoma (OSCC) Chemoprevention

Monday, 27th April - 10:06: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 20

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Introduction: Risk factor behavior e.g. smoking with/without alcohol or diseases associated with DNA repair deficits e.g. Fanconi anemia (FA) render the entire oral cavity at risk to develop OSCC. While systemically-delivered chemopreventives should conceivably provide oral mucosal field-coverage, bioavailability issues and drug-related toxicities generated disappointing outcomes. In contrast, local delivery formulations can deliver therapeutically-relevant levels without systemic side-effects. This proof of concept study determined whether Janus nanoparticles are a viable field-coverage chemopreventive strategy. Due to IL6's vital role in OSCC development, tocilizumab was selected as the payload chemopreventive.**Methods:1)** Formulation of tocilizumab-containing PLGA-chitosan nanoparticles (electrohydrodynamic co-jetting), **2)** Determination of keratinocyte [FA-OSCC and E6/E7 transduced (epi) human cell lines] Internalization via confocal microscopy and fluorescent-activated cell sorting (FACS), **3)**Assessment of nanoparticle-delivered tocilizumab immunoreactivity (tocilizumab ELISA), **4)**Evaluation of fluorescent-tagged nanoparticle penetration of oral mucosal explants (fluorescent microscopy). **Results:1)** JNP were successfully formulated to achieve 65% tocilizumab loading and subsequent release of immuno-reactive tocilizumab (ELISA confirmed)., **2)** Qualitative (confocal microscopy) and quantitative (FACS) analyses confirmed human keratinocyte nanoparticle internalization in a time-dependent fashion. Notably, even the shortest co-incubation FACS time point (1 h) revealed appreciable internalization (75% and 73% of epi and FA-OSCC cell populations, respectively)., **3)** Fluorescent-tagged nanoparticle studies revealed 85% of the mucosal explants (11/13) demonstrated particle penetration past the stratum corneum while 38% (5/13) contained nanoparticles in the basilar third of the epithelium. **Conclusions:**One of the mechanisms by which nanoparticles penetrate stratified epithelium is energy dependent (transcytosis). It is therefore probable that JNP optimization combined with in vivo analyses in ATP-replete tissues will enhance nanoparticle transport to the targeted, proliferative epithelial cells. Previously, our lab has shown that local injections of tocilizumab significantly reduced OSCC tumorigenesis in vivo. Studies are currently ongoing to determine the OSCC chemoprevention efficacy of locally injected, sustained-release tocilizumab JNP.

Case report: Persistent Herpes Simplex in an HIV patient with myositis and numerous eosinophils

Monday, 27th April - 10:30: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 76

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The herpesviruses are DNA viruses that cause a variety of disease and infections in humans. The most common types of herpesviruses that affect humans include, herpes simplex 1 (HSV-1), herpes simplex 2, varicella zoster virus, Epstein-Barr virus, and cytomegalovirus. The oral findings and treatment of HSV-1 in immunocompetent patients are well documented. However, the presentation of oral HSV in immunocompromised patients can be challenging both diagnostically and therapeutically. We describe a 50-year-old male with a medical history of HIV, hepatitis C, diabetes, and hypertension who presented for evaluation of a necrotic ulcer of his right lateral and ven- tral tongue. A similar lesion had been biopsied approximately four months prior and diagnosed as herpes simplex virus infection. The area was re-biopsied given exponential increase in size of the lesion. Histopathologic exami- nation revealed ulcerated mucosa with numerous eosinophils. Scattered epithelial cells with VCE were identified, similar to the first biopsy in which immunohistochemical staining was positive for HSV. A diagnosis of ulceration with chronic mucositis, myositis and eosinophilia with evidence of persistent herpes simplex virus infection was rendered, with a comment suggesting that immunosuppression and myositis with eosinophils were likely contribut- ing to the nonhealing nature of the lesion. We herein explore the diverse presentation and management of HSV infection in immunocompromised patients.

A case of Tophaceous Pseudogout: A Rare Crystalopathy Particularly Afflicting the Temporomandibular Joint

Monday, 27th April - 10:42: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 54

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Introduction: Tophaceous pseudogout is a rare variant of CPPD crystal deposition disease presenting with a soft-tissue calcified mass. Temporomandibular joint is a common site of involvement of tophaceous pseudogout. Mutations in gene ANKH (inorganic phosphate transport regulator) are involved in crystal related inflammatory reactions.

Materials and Methods

We report a case of Tophaceous CPPD crystal deposition disease. A 77-year old female with no pertinent past medical or drug history, presented with persistent dull pain in her left TMJ and gradual change in occlusion over two years with intermittent trismus. Clinical examination revealed a left pre-auricular swelling with compression of the left EAC. CT imaging showed a radiopaque expansile mass encompassing the left TMJ. Surgical removal was performed together with alloplastic reconstruction using a TMJ Concepts Total Joint Replacement prosthesis.

Results

Microscopic examination revealed a low-grade cartilaginous proliferation with intensely basophilic calcified crys- tal deposits which were rhomboidal in appearance and polarized weakly. Few areas showed atypical, occasional binucleated chondrocytes interpreted as chondroid metaplasia. No significant bone or soft tissue invasion was identified. The clinical, histological and radiographic findings were consistent with tophaceous pseudogout (massive CPPD deposition with cartilaginous metaplasia). Post-operatively the patient was pain-free with normalized occlusion and function.

Conclusions

Distinction from other benign chondroid neoplasms such as osteochondroma, synovial chondromatosis which may mimic CPPD disease is important. Low grade chondrosarcoma should be excluded, especially in decalcified sec- tions from which the CPPD crystals may be lost leaving behind only the atypical features in metaplastic chondro- cytes. Tophi of gout needs to be discriminated too, where monosodium urate crystals are more needle shaped and negatively birefringent under polarized light microscopy, besides hydroxyapatite crystals which appear as non-birefringent clumps. Correct identification of the type of crystal deposition is paramount to the treatment of crystal arthropathy as the underlying metabolic disturbances may be quite specific.

Gingival fibroma: An emerging distinctive gingival entity with well-defined histopathology.

Monday, 27th April - 10:54: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 33

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INTRODUCTION: Gingival growths are mostly reactive and seldom exhibit significant true neoplastic potential. The typical etiology is local irritation from dental plaque/calculus, trauma as well as medication-related overgrowth. Such lesions are easily distinguished and categorized into diagnoses such as pyogenic granuloma, peripheral ossi- fying fibroma, peripheral giant cell granuloma, etc. We present a previously undescribed reactive gingival growth with unique histologic features and suggest the diagnostic term "gingival fibroma".

METHODS: An IRB approved retrospective review encompassing years 2010-19, of the University of Florida Oral Pathology Biopsy Service, was performed to select cases. Demographics, clinical data, and microscopic diagnoses were recorded and analyzed. Diagnostic criteria were established by four board-certified oral and maxillofacial pathologists and included: a prominent fibromyxoid background, variable cellularity, whorled, or storiform pattern of arrangement of the cellular elements, and absence of significant inflammation or vascularity, calcification, and/or odontogenic islands.

RESULTS: A total of 60 cases were found to meet all criteria and included in the study. The age range in years was 14 to 87 with the mean at 45.11 years. A striking 90% of female predilection was noted. Approximately 62% of cases were reported on the maxillary gingiva, followed by 38.3% in the mandibular gingiva. The lesions were more common in the anterior incisor regions by 66.7%, followed by 11.7% in the canine/first premolar areas. All lesions were treated by surgical excision and 6 cases recurred within 2-3 years of excision. In all cases, lesional tissue appeared to extend to the surgical base of the specimen.

CONCLUSION: We present 60 cases of a histologically unique entity occurring exclusively on the gingiva and introduce the diagnostic term "gingival fibroma" for these lesions. Further studies with adequate clinical follow-up may help understand the true clinical behavior of these lesions.

Influence of zoledronic acid in physicochemical and morphostructural parameters of bone and dental tissue of mice submitted to a jaw osteonecrosis model.

Monday, 27th April - 11:06: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 66

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Zoledronic acid (ZA) leads to structural and physicochemical changes in mineralized tissues. The aim was to an- alyze physicochemical and morphostructural properties of bone and dental tissue of mice submitted to a model of ZA-related osteonecrosis of the jaws (OJ). This is a 2x2 factorial design experimental study, considering sex (male/female) and treatment (ZA/Saline). Lower left 2nd molar (day 42) extraction was performed after three ad- ministrations (days 0, 7, 14) of ZA 1.0 mg / kg or saline (n=8/group), with another administration on 49th and eu- thanasia on 70th day. Histological analysis, computerized microtomography, three-point bending test and Raman spectroscopy were performed. ANOVA 2-way/Bonferroni test was applied ($p<0.05$). Treatment with ZA promoted histological alterations in femoral epiphysis and increased bone necrosis signs ($p <0.05$) at sites of exodontia. Be- sides, ZA groups presented a lower number and greater separation of bone trabeculae, and smaller ratio bone/tissue volume in alveolar trabecular bone. Females presented a lower value of these parameters. In femoral bone, sex and treatment factors exerted an independent influence in mechanical parameters, on the cross-sectional area, maximum load, moment of inertia and work to fracture ($p <0.05$), being lower in females and increased in treated animals, which also presented higher flexural stiffness. Yield stress and flexural modulus were higher in females and lower with ZA treatment ($p <0.05$). Spectroscopic analysis showed increased crystallinity with ZA in cortical and medullar of right and left hemimandible, respectively, as well as femoral cortical. There was an increase of crys- tallinity in dental enamel and dentin with treatment. It is concluded that treatment with ZA, although associated with occurrence of OJ, modifies bone and dental mineral matrix, contributing to tissue biomechanics' improvement. Females present differences in femoral biomechanical properties and have a lower density of trabecular bone in the post-dental extraction socket, when compared to males.

ORAL SQUAMOUS CELL CARCINOMA IN PATIENTS UNDER THE AGE OF 30, A LARGE CASE SERIES

Monday, 27th April - 11:18: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 51

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Introduction: Oral squamous cell carcinoma (OSCC) is typically associated with older adults often with established relationship to tobacco and/or alcohol abuse. OSCC is rare in children and young adults without traditional risk factors. This case series encompasses an archival review of OSCC affecting patients under 30 years of age with analyses of demographics, clinical presentation, and histologic findings. **Materials and Methods:**An IRB approved study queried the archives of the UF Oral Pathology Biopsy Service from 1994-2019. All cases of OSCC affecting patients under 30 years were identified. Age, gender, location, clinical presentation, diagnosis, and grading were recorded, and slides were reviewed for diagnostic consensus. **Results:** During this span only 30 cases (0.76%) were identified in patients under 30 years of age out of a total of 3971 OSCC cases. Males (53.33%) were affected more commonly. An age range of 8 to 30 years with a mean of 24 years was noted. Only 3 were known smokers. In descending order, the lateral tongue, ventral tongue, and maxillary gingiva were most frequently involved. A wide spectrum of clinical diagnoses were obtained most consisting of reactive lesions. A few clinicians considered dysplasia and OSCC. Symptoms including pain, burning, swelling or dysphagia were present in 65.6% of cases. The histologic grade ranged from well to poorly differentiated. Perineural invasion was noted in 28.13%. Three out of 4 cases with P16 immunostaining at the time of sign out were positive. **Conclusion:** This study underscores the rare occurrence of OSCC in children and young adults. This may potentially lead to low clinical suspicion, misdiagnosis, and failure of prompt treatment. Further longitudinal multicenter studies with detailed medical history, treatment, and prognostic data may cast light on better understanding of the etiology of OSCC in young patients, aid prevention, and improve outcomes.

The histological stromal inflammatory subtypes and its transcriptional immune signature defined in oral squamous cell carcinoma with the soluble Semaphorin 4D immune biomarker

Monday, 27th April - 11:30: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 87

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Oral squamous cell carcinoma (OSCC) is a disfiguring malignancy that occurs in close proximity to vital structures, sometimes with limited treatment options. Thus, the recent immunotherapy treatment is a promising alternative. The peri-tumoral stromal inflammatory profile (PTSIP) has shown to be an important factor in determining patient's response to immunotherapy. Soluble biomarkers are a promising tool that can monitor the status of PTSIP and serve as a diagnostic method of the histological inflammatory stromal (HIS) subtypes. Semaphorin 4D (Sema4D) is a soluble immune biomarker that we previously detected in OSCC patient's plasma. *The objective* of this work is to define the HIS subtypes in OSCC according to the status of the PTSIP and assess the diagnostic potential of the soluble Sema4D (sSema4D) in peripheral blood, to identify OSCC HIS subtypes.

Findings: According to University of Maryland institutional review board approval, in a cohort of eighty excisional OSCC tumor tissue biopsies, we described the three HIS subtypes; inflamed (hot), the immune excluded and the deserted (cold). Immune focused gene expression analysis of the IFN-γ signature using representative tumor samples of the three HIS subtypes was described. We also analyzed sSema4D in plasma of the same eighty OSCC patients, using healthy donors and chronic inflammation/ autoimmune/ allergy patients as controls. High sSema4D levels (HsS4D) in plasma of OSCC correlated directly with the immune excluded HIS subtype (p=0.0001). HsS4D in blood clustered with low IFN-γ tumor immune signature (TIS).

Conclusions: Our data demonstrates the histological inflammatory subtypes and the corresponding transcriptional immune signature in OSCC. It highlights sSema4D as an immune biomarker that can be diagnostic of the tumor stromal inflammation. These findings open new avenues for advancing personalized immunotherapy in OSCC.

Progression to malignancy in oral potentially malignant disorders: A retrospective study of 5110 patients

Monday, 27th April - 11:42: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 88

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Introduction: Oral potentially malignant disorders (OPMD) have a reported prevalence of 1-5% worldwide and are associated with an increased risk of cancer development. OPMD may show epithelial dysplasia on biopsy. Certain clinicopathologic factors have been shown to affect risk of malignant transformation in OPMD, including: age, anatomical site, clinical appearance, smoking status and dysplasia. The objective of this study was to characterize the clinicopathologic features of OPMD with epithelial dysplasia (OED) that are associated with the development of oral squamous cell carcinoma (OSCC) in a large population-based cohort of Canadian patients. Materials and Methods: This is a retrospective study of 5110 patients, who were diagnosed with oral epithelial dysplasia or atypical verrucal-papillary proliferations between 2001 and 2015 from the archives of the Oral Pathology Diagnostic Services at Western University and University of Toronto. The cohort was matched with records from Cancer Care Ontario from 2005 to 2015 to determine progression to cancer. Results: 6.1% of patients developed OSCC within an average time of 2.9 years. The average age at cancer diagnosis was 61.2 years (SD 12.6 ± 25-94). Older age, non-smoking status, location on the tongue and presence of severe dysplasia/carcinoma in situ were associated with the development of OSCC. Conclusions: We have analyzed one of the largest population-based cohorts of OPMD to date. Our findings on risk factors for progression to cancer will contribute to our understanding of the management of OPMD.

Analysis and comparison of podoplanin (D2-40) and p53 as potential predictors of malignant progression in proliferative verrucous leukoplakia (PVL).

Monday, 27th April - 11:54: Oral Essay Programs - Oral (Student/Resident) - Abstract ID: 46

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Introduction: p53 overexpression is well documented in premalignant lesions of the oral cavity. However, recent studies have shown increased expression of podoplanin (D2-40) in oral dysplasia. This study aims to evaluate the efficacy of both markers in predicting malignant transformation in cases of proliferative verrucous leukoplakia (PVL), a recalcitrant oral premalignant condition with a high rate of malignant transformation. **Materials and methods:** With IRB approval the UF archives were searched from 1994-2019 for cases with clinical diagnosis of PVL with at least one biopsy and follow-up of at least 3 years. Included cases were tested for IHC reactivity to p53 and D2-
40. Reactivity was evaluated for basal cell layer nuclear positivity to p53 and cytoplasmic positivity to D2-40. Results for both tests were recorded as either >25% or <25% positivity in the basal cell layer. **Results:** A total of 17 cases were included. The mean age was 63.11 years and 76.4% of the patients were females. Locations included gingiva (59%), tongue (17%), buccal mucosa (12%), palate and floor of the mouth (6% each). The histological diagnoses included verruco-papillary hyperkeratosis/verrucous hyperplasia (59%), atypia/dysplasia (18%), hyperkeratosis (17%), and atypical epithelial proliferation (6%). Of the included cases, 7 (41%) subsequently developed malignancy. There was no statistically significant difference in terms of age, gender, location, or histologic diagnosis regarding either p53 or D2-40 positivity. There was no significant difference between p53 positivity between cases with or without malignant transformation; however, cases with subsequent malignant transformation demonstrated significantly higher positivity to D2-40 than those that did not transform ($p=0.006$, chi-square). **Conclusion:** D2-40 IHC testing was more useful in predicting malignant transformation than p53 in this small sample of PVL cases. Additional larger scale studies will likely confirm utility of D2-40 IHC testing in predicting PVL progression.