



American Academy of Oral  
& Maxillofacial Pathology

## | Essay Program

**Monday – June 25, 2012**

**8:00 am – 1:00 pm**

# Essay Abstracts – Monday, June 25, 2012

## #1 – 8:00 am

**EBV AND CD30 POSITIVE MUCOCUTANEOUS ULCERS OF THE ORAL CAVITY, AN UNUSUAL ENTITY: A SERIES OF 3 CASES** L Montague, D Cohen, I Bhattacharyya University of Florida, Gainesville  
Introduction: Epstein-Barr virus positive mucocutaneous ulcer (EBVMCU), related to immunosuppression, has recently been proposed as a distinct clinicopathologic entity by Dojcinov et al. (2010). These lesions are seen in older adults and present as ulcerations of the oropharyngeal mucosa and skin. Aim: We present a series of 3 cases of oral ulcerations arising in patients with a history of immunosuppression or immunosenescence. We discuss the clinical, histologic and immunohistochemical (IHC) features and compare our findings to reported cases of EBVMCU. Case 1: A 59 year old Caucasian male with a history of lymphoma and chemotherapy presented with gingival ulcers in all quadrants of 6 months duration. Case 2: A 41 year old Caucasian female with a history of methotrexate use presented with a 2 month history of a retromolar region ulcer. Case 3: An 83 year old Asian male with no history of immunosuppression presented with an ulcer of the maxillary vestibule of 1 month duration. Histology: Biopsies of lesions were characterized by a polymorphous inflammatory infiltrate and variable numbers of large atypical B-cells and Reed-Sternberg-like cells, which were EBV and CD30 positive and CD3 negative. A similar histomorphology and IHC profile can be seen in the Hodgkin lymphoma-like variant of lymphoproliferative disorders defined by the WHO as “other iatrogenic immunodeficiency-associated lymphoproliferative disorders”. While these Hodgkin-like lesions frequently occur at extranodal sites, there are limited reports of isolated oral ulcerations. Conclusion: We believe unusual ulcers in adult patients with history of immunosuppression should be evaluated with this entity in mind and when appropriate histologic findings are present, stains for CD30 and EBV should be performed.

## #2 – 8:12 am

**ROLE OF HIGH RISK HUMAN PAPILLOMAVIRUS INFECTION IN ORAL EPITHELIAL DYSPLASIA** C McCord, RJ McComb, G Bradley University of Toronto  
Background: Human papillomavirus (HPV) infection is a causative factor in a subset (70%) of oropharyngeal squamous cell carcinomas. Recent evidence suggests that the prevalence of HPV in oral squamous carcinoma is low (<10%). The relationship between HPV infection and progression from epithelial dysplasia to carcinoma has not been extensively studied. Objective: To detect high risk (HR) HPV in oral epithelial dysplasia and correlate with clinicopathologic features. Methods: 40 consecutive cases of high-grade oral epithelial dysplasia and 37 cases of low-grade dysplasia were examined for p16INK4a (mtm labs, MA) expression by immunohistochemistry. p16 is a sensitive marker for HR HPV infection. Cases demonstrating strong, diffuse nuclear and cytoplasmic staining in the dysplastic epithelium were considered positive. All p16 positive cases were studied further using in-situ hybridization for HR HPV (Ventana Inform HPV III Family16 Probe). Cases were HPV positive if unequivocal intranuclear hybridization signal was present within lesional epithelium. Results: HPV 16/18 was detected in 7 of 40 high-grade dysplasias (17.5%), and no low-grade dysplasias. HPV was significantly associated with high-grade dysplasia ( $p=0.01$ ). Five of 7 (71.4%) HPV-positive dysplasias involved the floor of mouth/ventral tongue. The relationship of HPV infection and anatomical site was statistically significant ( $p=0.04$ ). Age and sex showed no significant association with HPV infection. Conclusion: HR HPV is rarely detected in oral epithelial dysplasia, but when present shows significant association with grade of dysplasia and site.

# Essay Abstracts – Monday, June 25, 2012

## #3 – 8:24 am

**ASSESSMENT OF MATRIX METALLOPROTEINASE LEVELS IN HEALTHY HUMAN CONTROLS: PRELIMINARY DATA RELATED TO DOXYCYCLINE TREATMENT IN PATIENTS WITH VESICULOEROSIVE DISEASES** T Jhamb, JM Kramer, JE Fantasia Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY Oral vesiculoerosive diseases (VED) include chronic processes such as cicatricial pemphigoid (CP) and lichen planus (LP). Currently, therapy consists of immunosuppressive agents that demonstrate variable efficacy and cause potentially serious side effects. Enzymes that affect the integrity of collagen and modulate inflammation, such as matrix metalloproteinases (MMPs), may be therapeutic targets in VED. Increased expression of MMP 2 and 9 has been observed in human inflammatory diseases. Upregulation of MMPs has been documented in oral ulcerative disease; although the role of MMPs in the oral VED is poorly understood. Treatment with subantimicrobial dose doxycycline (SDD) inhibits MMPs specifically and is already used for the treatment of other chronic inflammatory processes. **HYPOTHESIS:** MMP 2 and 9 are detectable in the sera, saliva, and urine of healthy subjects. Detection and quantification will allow for the assessment of normal levels to be used for comparative purposes. **METHODS:** ELISAs were used to establish baseline levels of these MMPs in serum, saliva, and urine of healthy controls. **RESULTS:** Preliminary data indicate that MMP 9 is detectable in control sera (mean = 707.0 ng/mL +/- 220.6) and saliva (mean = 967.8 ng/mL +/- 706.6) with lower amounts present in urine (mean = 2.0 ng/mL +/- 3.1). MMP 2 was detectable in sera (mean = 164.2 +/- 40), but was not in saliva or urine. **CONCLUSION:** These results indicate that ELISAs can be used to evaluate potential differences between MMP 2 and 9 levels in healthy controls. Further studies are underway to investigate whether SDD reduces the expression and activity of MMP 2 and 9 in VED both locally and systemically.

## #4 – 8:36 am

**DENTINOAMELOBLASTOMA: A CASE REPORT AND NOSOLOGIC DISCUSSION REGARDING THE ENTITY** D Klingman, H Evans, KJ Penna ,JE Fantasia Hofstra North Shore-LIJ School of Medicine, New Hyde Park, NY Nassau University Medical Center, East Meadow, NY **Background:** The dentinoameloblastoma (DA) is a rare odontogenic tumor. One case of DA has been reported and is characterized by induction of dentinoid by neoplastic odontogenic epithelium without enamel formation. **Observations:** A 44 year-old man presented with an expansile mass of the right anterior mandible. The lesion caused facial asymmetry and effacement of the mandibular vestibule. Panoramic radiograph and computer tomography imaging revealed a large radiodensity of the right anterior mandible causing lingual and marked buccal expansion. There was a radiolucent rim surrounding the radiodense central component. Microscopic examination of the resected specimen revealed hypercellular zones of odontogenic epithelium with focal areas of peripheral palisading consistent with ameloblastic differentiation. This epithelium was intimately associated with an amorphous eosinophilic product consistent with a dentin-like material; dentinal tubules were not observed. The overall histopathology suggested dentinoid induction by tumor cells. Enamel matrix and epithelial ghost cells were not identified, thus excluding other recognized odontogenic tumors. A diagnosis of DA was rendered. Treatment consisted of mandibulectomy without continuity defect and reconstruction with autologous and allogeneic graft, bone morphogenic protein and titanium mesh. **Conclusions:** The clinical, imaging, and histopathological characteristics of DA are described. The DA is classifiable as a mixed odontogenic tumor exhibiting epithelial and mesenchymal components; separate and distinct from odontoameloblastoma, dentinogenic ghost cell tumor, and other odontogenic tumors with a mineralized component.

# Essay Abstracts – Monday, June 25, 2012

## #5 – 8:48 am

**THE IMPACT (OR LACK THEREOF) OF A THIRD HISTOLOGIC SECTION ON SAMPLING ERROR IN INTRA-OPERATIVE EVALUATION OF HEAD AND NECK SPECIMENS** JM Bastaki, BM Purgina, LT Wiehagen, RR Seethala University of Pittsburgh, PA Margin status in head and neck (H&N) cancer is a strong predictor of local control and outcome. Intraoperative consultation is useful in obtaining negative margins, but can occasionally show discrepancy with final margin status, typically due to sampling error. The literature suggests that increasing the number of sections per specimen may reduce this form of error. We thus compared the frozen-permanent discrepancy rate resulting from sampling error between 2005-2008 when the standard number of sections was two per specimen (2s) and 2008-2011 with a standard of three sections per specimen (3s). 96 discrepancies were found in 15,840 H&N frozen section parts (0.61%), of which 65 (67%; 0.42% of total volume) were due to sampling error. Of these sampling discrepancies, 41 (63%; 0.26% of total volume) occurred on margins. Overall error rate was slightly lower in the 3s period (42/8350, 0.50%) than in the 2s period (54/7490, 0.72%) but this difference was not significant (Pearson chi square  $p=0.08$ ). But somewhat surprisingly, the proportion of sampling errors was actually higher in the 3s period (33/42, 79%) as compared to the 2s period (32/54, 59%) ( $p=0.04$ ). A larger proportion of these sampling errors (24/33, 73%) were on margins in the 3s period than in the 2s period (17/32, 53%), though this difference was not significant ( $p=0.10$ ). Our findings suggest that sampling error on frozen sections is not necessarily reduced by increasing the number of sections per part, and that perhaps multiple parameters beyond simply number of sections may contribute to sampling error.

## #6 – 9:00 am

**CALCIUM PYROPHOSPHATE DIHYDRATE DEPOSITION DISEASE INVOLVING THE TEMPOROMANDIBULAR JOINT** A Ritchie, N Freuen, S Ruggiero, M Schwartz, J Fantasia Hofstra North Shore-LIJ School of Medicine, New Hyde Park NY Background: Calcium pyrophosphate dihydrate (CPPD) crystal deposition disease is a type of crystal forming arthritis with deposition of CPPD in the joint tissues. Deposition of CPPD often occurs in the articular tissues of the appendicular skeleton and less commonly the temporomandibular joint (TMJ). OBJECTIVE: To describe the clinical, imaging, gross and microscopic features of CPPD of the TMJ. OBSERVATIONS: A 52-year-old woman presented for evaluation of right sided pain in the TMJ region. Computerized tomography revealed a lesion arising in the joint space. The differential diagnosis included synovial chondromatosis, pigmented villonodular synovitis and chondrosarcoma. Surgical exploration confirmed the extent of disease, and tissues were submitted for frozen section. Florid rhomboid to square crystal deposition exhibiting weak birefringence with associated cartilage metaplasia was identified; a presumptive diagnosis of pseudogout was rendered. The TMJ including the glenoid fossa was resected with prosthetic joint reconstruction. Grossly, the surgical specimen revealed multiple small, white, chalky deposits involving all submitted tissues of the TMJ resection. The articular surface of the condyle was deformed. Microscopic features identified on frozen section were noted on the permanent sections, corresponding to the CPPD deposits noted grossly. Chondroid metaplasia was a striking feature with only focal areas of metaplastic bone identified. A focal giant cell and histiocytic reaction was noted in relation to some of the crystal deposits, but was not a prominent feature. CONCLUSIONS: CPPD is a rare crystal deposition arthropathy and can simulate other benign and malignant pathological processes, clinically, radiographically and microscopically.

# Essay Abstracts – Monday, June 25, 2012

## #7 – 9:12 am

### AGGRESSIVE YET BENIGN? THE SPECTRUM OF AMELOBLASTOMATOUS TUMORS

L Bowers, D Cohen, I Bhattacharyya University of Florida, Gainesville Malignancy is defined by the presence of any one or all of the following: anaplasia, invasion or metastasis. The ameloblastoma is considered a benign yet aggressive odontogenic neoplasm known to invade and destroy adjacent soft and hard tissue yet histologically it appears without the hallmarks of malignancy. Histologically benign ameloblastoma is reclassified as malignant when metastasis is detected and high-grade lesions of ameloblastic carcinoma may or may not metastasize. A reclassification scheme is proposed which would involve categorization of ameloblastomas according to histologic features, radiographic appearance, site and demographic features with the goal of alerting clinicians as to the potential biologic behavior of the individual ameloblastomatous tumor. Examples of various ameloblastomas, "atypical" ameloblastomas, ameloblastic carcinoma and metastatic/malignant ameloblastoma will be discussed along with a review of the literature

## #8 – 9:24 am

### ASSESSMENT OF KI67 AND P53 IN BENIGN VERSUS MALIGNANT AMELOBLASTIC TUMORS

R A. Abdelsayed, I. Stojanov, I. Zakjary Georgia Health Sciences University, Augusta Introduction: Ameloblastic tumors are relatively common and represent a continuum of histologic features and biologic behavior. These lesions are classified into histologically benign, conventional ameloblastoma (AB) and malignant (metastasizing) ameloblastoma (MAB), and ameloblastic carcinoma (ABC). Microscopically, the distinction between AB and MAB, in the absence of clinical and radiographic data, is not possible. However, microscopic diagnosis of ABC can be made, when there is sufficient cellular atypia, mitosis and tumor necrosis. Nevertheless, the distinction between ABC and the histologically benign lesions may be challenging at times. The intent of this pilot study is to assess the utility of Ki67 and P53 to examine whether they can be reliable in the distinction of these lesions. Methods and Material: Three cases of AB, one MAB and two ABCs were identified. Representative sections from each of the lesions were immunostained using Ki67 and P53. Quantification of positive and negative cells was performed using Bioquant NOVA Prime imaging analysis. Results: Ki67 stained 3.3-5.0%, while P53 stained 0.9-3.5% of cells in ABs. Ki67 stained 13.8% and P53 stained 2.1% of cells in MAB. However, in ABCs, Ki67 stained 55.5-65.8%, whereas P53 stained 40.7-56.2% of cells. In ABs, positive cells were confined to the peripheral ameloblast-like cells; while in MAB, there were positive central and peripheral cells. In ABCs, positive cells were distributed throughout tumor islands. Conclusion: Ki67 and P53 intensity and pattern of reaction may be used reliably to distinguish ABC from histologically benign ameloblastic lesions. However, these markers were unreliable in distinguishing AB from MAB, therefore; clinical and radiographic data are needed to make this distinction.

# Essay Abstracts – Monday, June 25, 2012

## #9 – 9:36 am

**DENDRITIC INTERSTITIAL CELLS AND MYOFIBROBLASTS IN THE STROMA OF SELECTED ODONTOGENIC LESIONS: A POSSIBLE CLUE TO CLINICAL BEHAVIOR** M Khalili, A Taheri Borujeni Ahvaz University of Medical Sciences Background and objective: Epithelial-stromal interactions are important in normal development and regeneration and have been shown to influence the growth potential of various tumors. CD34-positive dendritic interstitial cells (DICs) and myofibroblasts are two stromal cells that appear to be involved in regulation of tumor growth and invasion. The aim of this study was to evaluate and compare the distribution of these cells in the stroma of ameloblastoma, odontogenic keratocyst (OKC) and dentigerous cyst (DC) of the jaws. Materials and methods: 20 cases of ameloblastoma, 40 OKCs and 20 dentigerous cysts were selected according to the inclusion and exclusion criteria. 4 µm sections were cut from paraffin blocks and immunohistochemically stained with CD34 and alpha-SMA antibodies. The staining pattern was graded according to cell density and the percentage of stromal cells expressing the respective antigens was categorized as 0,+,+ + and + + + when up to 5%, between 5% and 25%, between 25% and 50%, or more than 50% of stromal cells stained positively. Data were analyzed with Chi-square and Fisher's exact tests. P<0.05 was considered as the limit of significance. Findings: The distribution of CD34 positive stromal cells in ameloblastoma was lower than DC and OKC. No significant difference was seen between DC and OKC. The distribution of myofibroblasts in ameloblastoma was significantly higher than DC and OKC. The difference between DC and OKC was not significant. Conclusion: Based on our findings, CD34 positive dendritic cells and myofibroblasts could be associated with clinical behavior in odontogenic lesions. According to the distribution of these cells in OKC, we could suggest a cystic rather than neoplastic nature for this entity.

## #10 – 9:48 am

**ORAL SQUAMOUS CELL CARCINOMA: EPIGENETIC AND MOLECULAR CHARACTERIZATION OF TUMOR INDUCED STROMATA (TIS) FORMATION AND ITS IMPACT ON TUMOR BEHAVIOR** W M Swelam, H Metwaly,, D Tamimi, T Saku College of Dentistry, Taibah University Al Madinah Al Monawarah, Saudi Arabia, College of Dentistry Tanta University Egypt College of Dentistry, Dammam University KSA, Graduate College for Medical and Dental Sciences, Niigata University, Japan Oral squamous cell carcinoma (OSCC); OSCC is one of the most serious malignancies worldwide. It attracts our attention that most of SCC tumor cell nests are surrounded by Juxta-cell nest zone of more hyalinized or myxoid nature when compared to normal stroma. Our aim is to elucidate the nature of these zones to characterize the origin of SCC tumor-induced stromata (TIS). Such specification of TIS can play a role in developing new strategies of SCC prognosis and treatment. To achieve our objective, we performed immunostaining and in situ hybridization for our 60 archived SCC cases including primary and recurrent/metastatic lesions. Cultured SCC and fibroblasts separately and in co-culture were subjected to immunofluorescent staining and RT-PCR of laser microdissected cells. Paraffin tissue sections were subjected to immunohistochemical staining for extracellular molecules of Tenascin and Heparan sulphate proteoglycan (HSPG)], endothelial cell markers, VEGF and VEGF receptors, in addition to endoglin/ CD105 correlated to expression of cyclin D1 and P300. A set of cultured ZK-1 and OF-1 cell lines was separately captured using laser microdissection and were subjected for RT-PCR at days 1, 3, 5, and 7 after seeding. Captured cells were subjected to RT-PCR for Tenascin, HSPG, and Fibronectin against GAPDH (housekeeping gene). Results clearly clarify the capability of SCC cells from tissue or in culture to synthesize its own stroma in the juxta- cell nest zone. Cells on the periphery of tumor cell nests were more active as indicated by proliferative markers and they have higher expression of CD105 that may indicate higher capability of these cells to undergo endothelial transition.

# Essay Abstracts – Monday, June 25, 2012

## #11 – 10:00 am

**EPITHELIAL TO MESENCHYMAL TRANSITION (EMT) AT THE INVASIVE FRONT OF HNSCC AND ITS ASSOCIATION WITH INVASION IN VITRO** J E Fox, K M Byrd, A L Willis, R M Castilho, S J Weiss, T E Danciu, University of Michigan, Ann Arbor    AIM: To study the expression of E-cadherin, vimentin, and Twist1 to gain a understanding of EMT in HNSCC, to determine if pattern of invasion is predictive of EMT, to investigate if Twist1 correlates with EMT, and to examine EMT biomarkers and their correlation with invasive behavior. METHODS: 15 cases of HNSCC were retrieved from the Oral and Maxillofacial Pathology Service. Pattern of invasion was assessed using Bryne's classification. E-cadherin and Twist1 immunoreactivity were evaluated on staining intensity and distribution. Vimentin immunoreactivity was noted as present or absent. HNSCC cell lines derived from patient tumors were evaluated for EMT markers by Western blotting and immunofluorescence. Invasive activity was assessed by culturing cells atop 3-D type I collagen matrices in cell culture inserts. RESULTS: Aberrant E-cadherin staining was observed at the invasive front in all samples. 46% of tumors demonstrated vimentin positivity and 27% of tumors demonstrated strong nuclear Twist1 expression. Twist1-positive tumors exhibited strong vimentin positivity and loss of membranous E-cadherin staining. There was no correlation between pattern of invasion and immunohistochemical staining of the 3 markers. All tumors aberrantly expressed at least one EMT marker, although high vimentin and Twist expression were not necessarily observed in cases with morphological changes suggestive of EMT. In cells from oral cavity SCC, high Twist1 expression coupled to high vimentin and loss of E-cadherin correlated with collagen-invasive activity in vitro. CONCLUSION: Preliminary studies identify aberrant expression of EMT markers at the invasive front of HNSCC and suggest that high vimentin expression coupled to high Twist1 expression may play an essential role in tumor invasion.

## #12 – 10:12 am

**PATHOGENESIS OF ORAL LICHEN PLANUS: NEW FINDINGS ON THE CRITICAL ROLE OF TH17, TH0 AND TH2 CELLS IN THE DEVELOPMENT OF EROSION AND RETICULAR LESIONS** G Ficarra, DTesi, R Biagiotti, L Lombardelli, F Logiodice, O Kullolli, M G Giudizi, M-P Piccinni    Reference Center for the Study of Oral Diseases, AUOC Careggi & University of Florence, Italy, Department of Internal Medicine and DENO THE Center, University of Florence, Italy    The pathogenic role of Th17, an additional subset of CD4+ T helper cells beyond the traditional Th1, Th0 and Th2 cells, was investigated together with Th0, Th1 and Th2 cells in reticular (RL) and erosive lesions (EL) of Oral Lichen Planus (OLP), which is a chronic T cell mediated inflammatory disease with a T cell infiltrate preceding epithelial damage. M&M: 14 patients with OLP were studied. Healthy adjacent mucosa (HAM) was also analyzed. Quantization of mRNA for cytokine and transcription factors in RL, EL and HAM was measured using the QuantiGene 2.0 multiplex assay (Panomics, Fremont, CA, USA). IL-17A, IL-17F, IL-23 R, RORC (Th17-type cytokines, receptor and transcription factor) and IFN $\gamma$ , IL-4, IL-5, IL-13, GATA3 (Th0-type cytokine) mRNAs were increased in biopsies of EL whereas in biopsies of RL of OLP IL-13 and GATA3 (Th2-type molecules) mRNA were increased, when compared to HAM biopsies. IL-17A, TNF- $\alpha$ , GM-CSF, IL-6 (Th17-type cytokines), IFN- $\gamma$  and IL-5 (Th0-type cytokines) levels produced by CD4+ T cell clones generated from EL were increased compared to IL-17A, TNF- $\alpha$ , GM-CSF, IL-6, IL-5 and IFN- $\gamma$  produced by CD4+ T clones from HAM. A prevalence of Th17, confirmed by IL-17A, IL-17F and RORC mRNA expression of these T clones, and a prevalence of Th0 CD4+ T clones derived from EL, was shown, when they were compared to Th17 and Th0 CD4+ T cell clones derived from HAM T clones, whereas a prevalence of Th2 and a decrease of Th0 CD4+ T clones from RL, compared to Th2 and Th0 CD4+ T cell clones derived from HAM clones was observed. Moreover an increased of CD161 expression by IL-17-producing T clones derived from EL compared to IL-17-producing T cell clones generated from RL was observed. Thus, the critical role of Th17 and Th0 in EL and of Th2 cells in RL of OLP is presented.

# Essay Abstracts – Monday, June 25, 2012

## #13 – 10:24 am

EXPRESSION OF OSTERIX AND PERIOSTIN IN CEMENTO-OSSEOUS DYSPLASIA AS EVIDENCE FOR ITS PDL ORIGIN Y Cheng, Y Ren, J Wright, J Feng TAMHSC-Baylor College of Dentistry, Dallas, TX  
The etiology and pathogenesis of cement-osseous dysplasia (COD) are still unclear. Although most pathologists believe that it is of periodontal ligament (PDL) origin, no evidence beyond the histological features and its unique location has been provided to support this theory. Osterix (OSX) is an essential transcription factor that is expressed in osteoprogenitor cells and in cementoblasts. Periostin is a matricellular protein. In the jaw bones, periostin is only expressed in PDL and periosteum. In this study, we investigated the expression patterns of OSX and periostin with immunohistochemistry in various stages of COD. Based on clinical, radiographic and histological findings, two cases for each of the early-, mid- and late-stage COD were selected. OSX nuclear staining was found in the stromal cells and in cells incorporated in newly formed calcified matrix in the early- and mid-stages of COD, but not in the cells in sclerotic calcified masses in late-stage COD. Periostin was found in the stroma but not in the calcified matrix in all stages of COD. The co-expression of OSX and periostin in the COD lesional cells and stroma strongly suggest that COD is of PDL origin.

## #14 – 10:36 am

DOC2B PROMOTER METHYLATION IN ORAL CANCER TISSUES Raghu Radhakrishnan K Satyamoorthy S Prasad S Bhat Manipal College of Dental Sciences, Manipal University, Manipal, India  
The development of oral squamous cell carcinoma (OSCC) is a result of multiple molecular events triggered by various risk factors resulting in alteration in DNA methylation machinery, suggesting a role for epigenetic modification. In this study, we screened for differential methylation in human oral cancer DNA and compared it with its matched normal control using methylation sensitive arbitrarily primed polymerase chain reaction (MS-AP-PCR) assay. Several CpG rich fragments which were differentially methylated were identified, cloned and sequenced. The sequence identified in the promoter region of DOC2B gene spanning -376 to + 36bp, methylated in oral cancer tissues as confirmed by methylation sensitive dimethyl sulfoxide polymerase chain reaction (MS-DMSO-PCR) was further validated by busulfite genome sequencing (BGS). DOC2B promoter and other differentially methylated sequences characterized in our series may serve as diagnostic markers in human oral cancer.

# Essay Abstracts – Monday, June 25, 2012

## #15 – 10:48 am

**ANEUPLOIDY IN ORAL LICHEN PLANUS IS A CONSISTENT PHENOMENON IN HIGH-RISK PATIENTS** A Hirshberg, N Yarom, T Shani, I Kaplan, L Trakhtenbrot Tel-Aviv University Tel-Aviv, Israel, Rabin Medical Centre, Beilinson Campus, Petah-Tiqva, Israel, Cancer Research Center, The Chaim Sheba Medical Center, Israel Oral lichen planus (OLP) carries an increased risk for malignant transformation. In a previous study we have analyzed oral brush samples obtained from 57 patients with OLP. The samples were simultaneously analyzed for morphology and fluorescent in-situ hybridization (FISH) using chromosomes 2 and 8 centromeric probes. Aneuploid cells (ACs) were found in 16 patients (28.1%); in 10 (17.5%) over 5% of the cells were aneuploid. The aim of the present study was to show if the ploidy state of the patients persists over time. In 33 patients a second brush sample was obtained in a mean follow-up time of 43 months following the first analysis. 13 out of 16 patients with over 1% ACs detected in the first sample had over 1% ACs also in the second sample. ACs were detected in two patients in whom, the first sample was negative. In 15 patients, ACs were not found in both samples. The ploidy state of OLP is relatively consistent over time and can be used, therefore, as a reliable tool that can discriminate a subgroup of high-risk patients that require close follow-up for early detection of oral cancer.

## #16 – 11:00 am

**COMPARISON OF CD44 EXPRESSION IN INTRAORAL SALIVARY DUCTAL PAPILOMAS AND ORAL PAPILLARY SQUAMOUS CELL** S Fitzpatrick, L Montague, D Cohen, I Bhattacharyya University of Florida, Gainesville CD44 is a transmembrane adhesion molecule that is reported to be useful in the differentiation of benign and malignant papillary lesions. Previous studies have shown positive staining of CD44 in sinonasal papillomas and breast intraductal papillomas with loss of expression in invasive carcinoma allowing distinction between these similar appearing lesions. In addition, oral mucosal lesions have also demonstrated loss of CD44 in invasive carcinoma when compared to normal epithelium, hyperplasia, or oral squamous papillomas. To the best of our knowledge, no prior studies have compared variations in CD44 expression in salivary ductal papillomas when compared to oral papillary squamous cell carcinomas. In this study, 18 cases of intraoral minor salivary gland ductal papillomas and 19 cases of oral papillary squamous cell carcinoma were evaluated for expression of CD44. Within the ductal papilloma group, 6% showed absent staining to CD44, 33% weak staining, 60% moderate staining, and 0% strong staining with 76% diffusely expressing the stain and 24% focally expressing it. The papillary squamous cell carcinoma group showed 0% absent staining to CD44, 0% weak staining, 26% moderate staining, and 74% strong staining with 100% in a diffuse pattern. In conclusion, comparison of CD44 staining patterns between salivary ductal papillomas and oral papillary squamous cell carcinomas failed to exhibit reactivity as reported in previous studies performed on nasal and breast neoplasms. We hypothesize that the strong reactivity of CD44 in papillary squamous cell carcinoma noted in our study is probably attributable to the high level of differentiation that these lesions typically exhibit when compared to the papillary nasal carcinomas and papillary carcinomas of the breast.

# Essay Abstracts – Monday, June 25, 2012

## #17 – 11:12 am

**SUPERFICIALLY INVASIVE SQUAMOUS CELL CARCINOMA OF THE ORAL CAVITY** C Haberland, C Sasaki, B Judson, R Virk, M Prasad Yale-New Haven Hospital, CT Superficially invasive or microinvasive squamous cell carcinoma (SISCC) is a poorly defined entity in the oral cavity. The purpose of this study is to describe the clinical and histopathologic features of this lesion. We defined SISCC of the oral cavity as a horizontally spreading squamous cell carcinoma that develops from a carcinoma in situ or severe dysplasia with focal and/or superficial invasion of less than 2 mm and no deeper than the lamina propria. Twelve cases met these criteria. Clinically, there was an equal sex distribution (6M: 6F) and the average age was 53 years old (range 33-84). The most common location was the lateral tongue (n=8), followed by floor of mouth (n=2) and soft palate (n=2). Histopathologically, the average depth of invasion from the tumor surface to deepest point of invasion was 1.16 mm and measured from the nearest basement membrane to the deepest point of invasion was 0.53 mm. In 7 of the cases the tumor cells invaded <50% of the lamina propria. A moderate to severe lichenoid band-like lymphocytic response to the tumor was noted in 7 of the cases. Intracellular keratinization in tumor cells was observed in all cases but keratin pearls were seen in only 4. Only 2 cases were found to have a papillary surface. The nuclear grade was found to be severe (grade 3) in 8 cases. All cases were treated with surgical resection and only 4 cases received a modified radical neck dissection but no metastasis were found. The follow-up ranged from 1-18 years and there were frequent positive margins at surgery, and multiple recurrences, but no regional or distant metastasis. In summary, we describe SISCC of the oral cavity as a flat, minimally invasive, intensely immunogenic carcinoma with high-grade nuclei that are indolent but horizontally aggressive.

## #18 – 11:24 am

**SINONASAL RENAL CELL CARCINOMA-LIKE ADENOCARCINOMA** K Magliocca, Z Patel, J DelGaudio, S Budnick, S Muller Emory University The sinonasal renal cell carcinoma-like adenocarcinoma (SRCLA) is a recently characterized malignancy. A review of the English language literature reveals only four previously reported cases of SRCLA. We present two additional cases, the first presenting with chronic nasal obstruction and epistaxis in a 51-year-old male, and the second presenting as recurrent epistaxis in a 38-year-old male. Microscopically, the neoplasms were characterized by back-to-back ductal structures composed of cuboidal cells with a clear cell morphology. Cytologically, mild nuclear and cellular atypia were identified but abnormal mitoses were absent. A highly vascular stroma with delicate fibrous septae was identified between aggregates of neoplastic glandular epithelium. Immunohistochemically, both tumors stained positively for vimentin, CK-7 and S100. Neither tumor marked with RCC. PAX-2 was positive in the first case, but negative in the second case. The microscopic differential diagnosis, including metastatic renal cell clear cell carcinoma, clear cell neoplasms, squamous cell carcinoma with clear cell change and ectopic pituitary adenoma, will be highlighted. Pre-operative tumor embolization followed by wide local excision with close clinical follow-up appears to be the treatment of choice; however, these recommendations are limited by the rarity of the neoplasm and a relatively short follow-up period of the available case material.

# Essay Abstracts – Monday, June 25, 2012

## #19 – 11:36 am

**MAMMARY ANALOGUE SECRETORY CARCINOMA OF LABIAL SALIVARY GLANDS** F Kratochvil J Stewart Oregon Health & Science University, Portland Mammary analogue secretory carcinoma of salivary glands (MASC) is a recently described distinctive salivary gland neoplasm. Similar to rare secretory carcinomas of the breast, MASCs have microscopic features resembling both acinic cell carcinoma and low-grade cystadenocarcinoma of salivary glands with a lobulated growth pattern demonstrating cystic and microcystic spaces filled with eosinophilic secretory material. The tumor cells generally stain weakly for periodic acid-Schiff with diastase and are positive for S100 protein and strongly positive for vimentin. Also like their counterpart in the breast, these tumors are characterized by a t(12;15) (p13;q25) ETV6-NTRK3 translocation. In the past year we have encountered two such tumors in the upper and lower lips, both of which had relatively weak periodic acid-Schiff staining with diastase and were positive for vimentin and S100. Fluorescence in situ hybridization (FISH) was performed on both tumors with the ETV6 break-apart probe showing disruption of ETV6 (12p13). Microscopic criteria as well as the clinical significance for the diagnosis of MASC will be discussed.

## #20 – 11:48 am

**RETROSPECTIVE DIAGNOSIS OF NUT MIDLINE CARCINOMA** L Solomon, K Magliocca, S Muller Emory University Atlanta, GA Background: NUT midline carcinomas (NMC) are aggressive tumors arising primarily in the head, neck and mediastinum in young individuals. NMC exhibits a chromosomal translocation resulting in overexpression of nuclear protein in testis (NUT), previously only detected by FISH. An extensive survey for NMC in a series of poorly differentiated carcinomas of the upper aerodigestive tract has not been previously reported. Design: The EUH pathology database from 2003-2012 was queried using the search terms: undifferentiated, carcinoma (Ca), poorly differentiated, nasopharyngeal, thymic, sinonasal, mediastinal; tumors for which another primary site was identified were excluded. Diagnosis of NMC was based on strong diffuse nuclear immunohistochemical (IHC) staining with rabbit monoclonal antibody NUT (C52B1) (Cell Signaling Technology, Inc., Danvers, MA, USA). Results: 47 cases with material available for testing included 18 poorly differentiated Cas, 6 non-keratinizing Cas, 4 undifferentiated Cas, 5 sinonasal undifferentiated Cas (SNUC), 2 sarcomatoid Cas, 3 thymic Cas, 2 poorly differentiated non-small cell Cas, 2 high grade adenocarcinomas, 2 intermediate grade mucoepidermoid Cas, and 1 each: epithelial malignancy, pituitary Ca, poorly differentiated basaloid Ca. Patients average age was 54.9y (range:16-82), with 19 women & 28 men. A single case of NUT translocation was detected in a 26 y old man with a left nasal and maxillary sinus tumor diagnosed as poorly differentiated Ca with neuroendocrine features and focal squamous differentiation. Conclusions: In this series a NUT translocation was detected in 5.6% of poorly differentiated Ca cases of the head & neck and establishes a basis for the inclusion of NUT monoclonal antibody in diagnostic IHC panels.

# Essay Abstracts – Monday, June 25, 2012

## #21 – 12:00 pm

**THE FREQUENCY OF BENIGN AND MALIGNANT TUMORS IN ULCERATED VERSUS NON-ULCERATED EXOPHYTIC LESIONS OF ORAL MUCOSA** | Allon DM Allon G Chaushu I Kaplan  
Goldschleger School of Dental Medicine, Tel-Aviv University, Israel Rabin Medical Center, Tel-Aviv Israel  
Objectives: Investigate the spectrum of pathologies in ulcerated versus non-ulcerated exophytic lesions of oral mucosa. Methods: Retrospective analysis 2009-2011. Results: The analysis included 713 biopsies. There was a wide age range, 9.6% of patients < 20 years, 29.1% 20-50 years and 61.4% >50, with a female predominance (44.9% M, 55.9% F),  $p=0.02$ . 91.5% of lesions were non ulcerated, 8.5% ulcerated. 69.6% of all lesions were reactive, 21.3% benign tumors, 7.8% malignant tumors and 1.3% premalignant. A significant difference in the distribution of lesions was seen between the ulcerated and non-ulcerated groups: in the ulcerated group 48.3% were reactive, 15% benign tumors and 35% malignant, in the non-ulcerated 70.4% were reactive, 21.9% benign and 5.2% malignant tumors,  $p<0.0001$ . An age related increase in the frequency of malignant tumors was noted, from 3.0% in the below 20 age group to 11.1% in the over 50 group, while the frequency of benign tumors was almost constant 23.9% - 22.9% respectively,  $p<0.0001$ . Conclusions: Approximately 1/3 of the exophytic lesions were neoplastic. The chances of an ulcerated mass to represent a malignancy are significantly higher than a non-ulcerated one, especially in patients over 50. Nevertheless, 5.2% of the non-ulcerated lesions harbor a malignancy, which may be missed if only surface ulceration is considered a disturbing clinical sign. These results strongly support the importance of removing and submitting for microscopic analysis all exophytic lesions of the oral mucosa, regardless of surface ulceration.

## #22 – 12:12 pm

**SURROGATE MARKERS: THE DIF ALTERNATIVE FOR FORMALIN FIXED/PARAFFIN EMBEDDED SPECIMENS** R Eversole Oral Pathology Diagnostic Services, San Diego, CA  
Background: Coupled with routine histopathologic assessment, direct immunofluorescence (DIF) provides confirmatory diagnostic findings for immunopathic desquamative diseases of skin and mucosa. The DIF antibody markers do not recognize the appropriate epitopic targets on formalin fixed tissues. DIF requires special transport media fixation, frozen sections, frequent repeat biopsy and a fluorescence microscope. This communication describes surrogate immunomarkers that can be employed on formalin fixed current and archived specimens. Material and Methods: Fifteen archived fixed cases each of pemphigus vulgaris (PV), mucous membrane pemphigoid (MMP), erosive lichen planus (ELP) and varying numbers of rare oral bullous diseases were assessed by standard immunoperoxidase methodology using three primary antibodies reactive with epitopes on 1. Keratinocyte pericellular membrane bound Ig (AB001), 2. Lamina lucida basement membrane bound complement (AB002) and 3. Basement membrane bound fibrin products (AB003). These antibodies were selected after screening a variety of immunomarkers for reactivity. Results: 14 of 15 cases of PV, 15 of 15 cases of MMP and 13 of 15 cases of ELP mirrored results seen with DIF (i.e.: AB001, pericellular and AB002 pericellular positivity for PV, AB002 basement membrane positivity for MMP and AB003 basement membrane positivity for fibrin products. Conclusion: Selected immunomarkers directed to autoantibodies that are in vivo bound to host antigens in formalin fixed/paraffin embedded lesional specimens can replicate patterns seen with direct immunofluorescence.

# Essay Abstracts – Monday, June 25, 2012

## #23 – 12:24 pm

**REACTIVE EXOSTOSIS: CLINICOPATHOLOGY OF 27 LESIONS; COMPARISON WITH TORI AND BUCCAL EXOSTOSIS** J Bouquot, G Welch, P Suarez, S Zarghouni University of Texas, Houston  
Background: Reactive cortical lesions can have a rapid onset & alarmingly active histopathology, as opposed to the much more common, histologically more mature & less alarming tori & buccal exostoses. Maxillofacial reactive exostosis (RE) is not rare, we think, but is virtually unreported except for the very specialized variant, subpontic osseous hyperplasia. Objective: To clinicopathologically characterize, for the first time, a series of RE lesions. Methods: 27 cases and 32 controls (tori and buccal exostoses) were derived from 2 surgical pathology services. Results: Average subject age at diagnosis was 38 years (range: 27-51), compared to 52 years for controls (range: 38-69). Lesions were located on the non-midline hard palate (n = 13), facial surfaces of the posterior mandible (n = 6) or maxilla (n = 3) and beneath pontics (n = 4); 1 occurred on the lingual surface of the ramus. Lesions averaged 11 mm in diameter (range: 4-28 mm). Mild pain/tenderness was associated with 6 lesions; overlying mucosa was not erythematous or ulcerated. Average duration was 9.3 months. Local trauma or inflammation, e.g. adjacent to dental fistulae, was considered causative in 14 cases and in the 4 subpontic lesions; all other lesions had no obvious cause. All cases showed large areas of new bone formation, primarily woven and immature lamellar bone. All cases showed active osteoblasts and fatty marrow was seldom seen. Controls showed much more mature bone, increased bone density, minimal osteoblastic activity, abundant marrow and minimal fibrosis. Chronic inflammatory cells were seen in 14 cases but in none of the controls. Conclusion: The Clinicopathology of RE differs considerably from tori and buccal exostoses. RE apparently remains histologically immature for months, perhaps years.

## #24 – 12:36 pm

**PITFALLS IN FORENSIC ODONTOLOGY: REVIEW WITH ORIGINAL RESEARCH ON GENDER IDENTIFICATION GENES** R George Melaka Manipal Medical College, Melaka, Malaysia The reliability of forensic evidence lies in its accuracy; even though the conventional methods of investigation in forensic odontology are much refined, the investigator must be aware of the pitfalls in each of these methods. The limitations and possible errors that can occur commonly during forensic dental investigations are reviewed in this paper along with original study done on genes of forensic gender identification. Gender of 37 subjects was identified accurately by detection of SRY gene with real time PCR, using exfoliated epithelial cell adhered on acrylic dentures as the source of DNA, as an alternate to the commonly used Amelogenin gene to get unambiguous results. Regardless the technologies used for gender identification the result may be erroneous in certain conditions. This paper highlights the pitfalls of forensic investigation and precautions that an investigator should be aware while collecting evidence and conducting forensic dental investigations.

# Essay Abstracts – Monday, June 25, 2012

## #25 – 12:48 pm

THE HEAD, NECK AND SYSTEMIC MANIFESTATIONS OF LEVAMISOLE-CONTAMINATED COCAINE USE K Magliocca, N Coker, D Parker, S Parker, C Mitchell, A Church Emory University, Atlanta University of Florida Gainesville Levamisole is a drug which was once utilized in the management of autoimmune diseases such as Behcet's disease, and rheumatoid arthritis. In 2000, this immunomodulating agent was removed from the market as a result of adverse cutaneous and hematologic effects in humans. The drug is still available as a veterinary anti-helminthic and has been detected in cocaine within the United States. A common clinical finding resulting from the use of levamisole tainted cocaine includes purpura of the earlobe and helix, but retiform purpura has been reported on the trunk and extremities with some frequency. Importantly, hematologic abnormalities such as agranulocytosis, is not uncommon. Some individuals develop oral ulcers, possibly as a consequence of neutropenia. The clinical differential diagnosis depends on the extent of the physical and laboratory findings but may include lupus erythematosus, anti-phospholipid antibody syndrome, erythema multiforme, Wegener's granulomatosis and even meningococcal vasculitis. This presentation documents the available clinical, laboratory and histopathologic findings of two new patients, aged 43 and 63 years, suspected of consuming levamisole-contaminated cocaine. The clinical, histopathological and laboratory findings will be discussed in addition to the approach to the diagnostic work-up designed to exclude other differential diagnostic entities.