

Oral Abstracts – *Tuesday, June 24*

#1 - Time presenting: 14:30 – Venetian Room (Lobby Level)

A REAL-TIME APPLICATION OF FLUORESCENCE VISUALIZATION (FV) TO IDENTIFY A NOVEL OPTICAL FIELD FOR SUBCLINICAL EXTENSION IN HIGH-RISK ORAL LESIONS. C. Poh, L. Zhang, S. Durham, D. Anderson, A. Kung, M. Rosin. University of BC, BC Cancer Agency & Research Centre, Vancouver. There is no consensus in managing high-grade dysplasia/carcinoma in situ (HGL). Frequent recurrence following excision implies the presence of subclinical change at the margins not-apparent at surgery, resulting in incomplete excision. FV has demonstrated the ability to identify clinically not-apparent oral lesions. The objective of this study is to apply this novel optical technology in the operating room to assess surgical fields for subclinical extension beyond clinical boundaries in high risk oral lesions. Among 35 lesions (22 HGLs and 13 SCCs) examined, FV alteration (FV loss, FVL) was noted in all lesions. For HGL, almost all (21/22; 95%) FVL was going beyond clinical boundaries. This uneven subclinical extension of FVL, ranging from 1 to 25 mm did not differ significantly from those of SCC. Strikingly, 35% (13/37) of biopsies from FVL boundary beyond clinical boundary of HGLs showed histologically high-grade change and 5 of them beyond 10-mm, the conventional margin set-up for cancer. Conclusion: Through identifying subclinical field change associated with high-risk histology, integrating FV in surgery might provide a useful approach to better manage HGL at the point of care and a subgroup of HGLs should be treated aggressively (sponsored by NIDCR R01 DE17013, CIHR MOP-77663 and MSFHR).

#2 - Time presenting: 14:42 – Venetian Room (Lobby Level)

TRANSDUCTIONAL RETARGETING OF ADENOVIRUS-5 TO $\alpha\beta6$ INTEGRIN FOR CANCER THERAPY. L. Coughlan, I. McNeish, G. Vassaux, JF. Marshall, IR. Hart and GJ. Thomas. Institute of Cancer, Barts and the London School of Medicine and Dentistry, UK. The epithelial-specific integrin $\alpha\beta6$ is an attractive target for tumour therapy since it is not expressed on normal epithelium, but is upregulated in many carcinomas, particularly oral squamous cell carcinoma (SCC) where it promotes tumour progression. The use and relative safety of adenoviral (Ad5) vectors for gene therapy has been well documented. However, low expression of the Ad5 receptor (CAR) on malignant tissue often renders it less susceptible to infection. The aim of this study was to redirect the tropism of Ad5 to infect specifically $\alpha\beta6$ -expressing SCC cells. Methods and Results: We previously characterised a peptide (A20) with high affinity and specificity for $\alpha\beta6$. We incorporated this peptide genetically into the HI loop of the Adenovirus-5 fibre protein. Recombinant fibre protein was expressed in E. Coli and purified. The ability of KnobA20 to bind and inhibit $\alpha\beta6$ -specific antibody (10D5) binding was confirmed by flow cytometry on a panel of high $\alpha\beta6$ -expressing cell lines. KnobA20 also was capable of inhibiting $\alpha\beta6$ -dependent effects in Transwell migration assays, abrogating SCC migration towards TGF- $\beta1$ latency-associated peptide at concentrations of 0.025 μ g/ml. An adenoviral vector, Ad5A20 was constructed, which demonstrated significantly increased infectivity ($p < 0.0001$) and enhanced cytotoxicity when compared with Ad5WT on a panel of four HNSCC lines. Infection was also blocked in the presence of 10D5. Dose-response cytotoxicity profiles for both Ad5WT and Ad5A20 were as follows: TR126 (EC50=0.051, 0.003), TR138 (EC50=0.302, 0.009), SCC25 (EC50=1.498, 0.054) and HSC-3 (EC50=4.689, 2.688). Conclusion: These data establish that retargeting of Ad5 to $\alpha\beta6$ -expressing cells may offer potential for the treatment of SCC.

Oral Abstracts – *Tuesday, June 24*

#3 - Time presenting: 14:54 – Venetian Room (Lobby Level)

RADIOMETRIC ANALYSIS OF PERIAPICAL LESIONS WITH AND WITHOUT ACTINOMYCES. R. Kuklani, M.K. Nair, D.M. Cohen, I. Bhattacharyya. U. of Florida, Gainesville. Introduction- Actinomycotic colonization is often identified in non-healing periapical biopsies and may be larger in dimension than lesions without actinomycetes. Aim- The purpose of this pilot investigation is to explore the feasibility of identifying potential radiometric differences in periapical radiolucencies with and without actinomycotic colonization using periapical radiographs, using histopathology for ground truth. Methods- Periapical radiographs of lesions with and without actinomycosis included in the study had been sent in by practitioners to the UF Oral & Maxillofacial Pathology Biopsy Service along with tissue specimens. All radiographs were imported as uncompressed TIFF (tagged image file format) files into an image processing program (TACTwb, Bowman Gray School of Medicine, Wake Forest U., Winston Salem, NC) as 8 bit images. The radiographs were standardized using reference measurements of the mesio-distal widths of the crowns, and apico-occlusal lengths of individual teeth (Wheeler™s Dental Anatomy, 8th Ed). The lesion sizes were measured for length and height using calibrated values based on known tooth dimensions. Repeat measurements were done and mean values obtained. The reading session was repeated after an interval of 2 weeks, and overall mean values were calculated. All measurements were made by a single observer. Results- The preliminary results reveal mean height of lesions with biopsy proven actinomycetes was 13.39 mm and mean length 16.76mm, while lesions without actinomycetes revealed a mean height of 10.62mm and mean length of 12.10 mm. Conclusion- The apical radiolucencies with biopsy proven actinomycetes maybe larger in dimension to those without bacterial colonization in this preliminary study. Further controlled studies are required in order to confirm this finding.

#4 - Time presenting: 15:06 – Venetian Room (Lobby Level)

SIALOLIPOMA IN LOWER LIP: CASE REPORT. N. Binmadi, R. Chaisuparat, B. Levy, N Nikitakis. U. Maryland, Baltimore. Sialolipoma is a relatively rare and newly described, distinct entity of benign salivary gland lipoma. The etiology of the sialolipoma is not completely understood. Any sites within the oral and maxillofacial region may be involved, with the parotid gland being the most common location. This report presents a case of 54 -year- old female who noticed a painless swelling in her lower lip. Biopsy and histopathologic examination of this tumor revealed an encapsulated mass consisting of mature adipose tissue, with central islands of salivary gland acini and ducts. Neither atypia nor mitotic figures were observed. The tumor was treated by surgical excision. The patient was disease free at the 2 year follow-up. We reviewed the clinical and histopathologic features of 21 previously reported cases of sialolipoma reported in English literature. Clinically, the lesions were solitary, painless, palpable masses; average size was 2.72 cm in diameter. Lesions showed a male predilection. Patient™s ages ranged from 7 weeks to 84 years, with an average of 50.85 years. The duration of the lesions ranged from two months to ten years, with average of three years. All cases were treated with surgical excision with no evidence of recurrent disease.

Oral Abstracts – *Tuesday, June 24*

#5 - Time presenting: 15:18 – Venetian Room (Lobby Level)

ASPERGILLUS MYCETOMA OF THE MAXILLARY SINUS: CASE REPORT AND REVIEW. D. Sundararajan, V. Noonan, M. Lackey, G. Gallagher, S. Kemp, S. Kabani. Boston U., Boston, Massachusetts. Chronic sinusitis is the most common chronic condition affecting the maxillary sinus. Fungi play a major role in chronic sinusitis. Paranasal fungal sinusitis is classified into two categories, invasive and non invasive forms. Aspergillus mycetoma (fungus ball or aspergilloma) of the maxillary sinus is a chronic non invasive mycosis that is commonly diagnosed in patients with a prolonged history of recurrent maxillary sinusitis. The fungus ball is formed when filamentous fungi colonize a previously formed cavity. It is composed of fungal hyphae, inflammatory cells, fibrin, mucus and amorphous debris. Chronic inflammation may be noted surrounding the fungus ball. Colonization is typically caused by Aspergillus species, the identification of which is aided by morphologic characteristics. Tooth extraction and endodontics in the posterior maxilla are considered to be predisposing local risk factors for developing a maxillary sinus fungus ball. We present a case of aspergillus mycetoma of the maxillary sinus in a 32 year old woman with a history of sinusitis. The panoramic radiograph showed a radiopaque lesion present in the left maxillary sinus. The left maxillary first molar was endodontically treated. The histological features of this interesting case will be presented along with a review of the pathogenesis, clinical presentation, diagnosis, treatment and prognosis.

#6 - Time presenting: 15:30 – Venetian Room (Lobby Level)

HISTOPATHOLOGICAL FEATURES OF CYTOMEGALOVIRUS INFECTION OF THE ORAL MUCOSA. M. Mansour, Y. Cheng and J Wright. Texas A&M Health Science Center Baylor College of Dentistry, Dallas, Texas.

Cytomegalovirus (CMV) is a virus of the herpes family. It typically causes an asymptomatic or mononucleosis-like infection in immunocompetent individuals as well as devastating systemic infections in neonates and in immunosuppressed patients. The most common oral manifestation of CMV infection is mucosal ulceration. The classic histopathological features for CMV infected cells have been described as having a distinctive large pink or purple intranuclear inclusion surrounded by a clear halo (owl eye) or less commonly, amphophilic cytoplasmic inclusions.

Here, we report 2 cases showing significantly enlarged endothelial cells and stromal fibroblasts with eosinophilic nuclear inclusions or purple granular nuclear inclusion bodies. No owl eye cell was identified. Immunohistochemical studies were performed to confirm the presence of CMV viral proteins in the enlarged cells and the endothelial cell origin of most of the infected cells. Enhanced awareness of the non-classic histopathological features of CMV infection is emphasized.

Oral Abstracts – *Tuesday, June 24*

#7 - Time presenting: 15:42 – Venetian Room (Lobby Level)

HYBRID CENTRAL ODONTOGENIC FIBROMA WHO TYPE WITH GIANT CELL GRANULOMA-LIKE LESION: CASE REPORT. R. Younis, M. Scheper, C. Lindquist, B. Levy. U. Maryland, Baltimore. Central odontogenic fibroma (COF) is a rare benign ectomesenchymal odontogenic tumor of the jaw bones. Only twelve cases of COF with giant cell granuloma (GCG)-like areas have been reported in the English literature. Here we present a new case of COF- WHO type- with a GCG-like component. A 57 year old female presented clinically with buccal expansion and a well defined unilocular radiolucency in the body of the mandible. Histologically, the lesion showed a unique mixture of odontogenic epithelial islands intermixed with multinucleated giant cells (MNGCs) in a highly cellular fibrous connective tissue stroma through out most of the lesion. Only a small portion of the lesion showed the typical histologic pattern of each component separately. Postitive immunohistochemical staining with pancytokeratin (CK) highlighted the odontogenic epithelial component merging directly with the GCG component. The significance of GCG-like areas within COFs is the risk of recurrence following curettage, possibly necessitating more aggressive therapy.

#8 - Time presenting: 15:54 – Venetian Room (Lobby Level)

CENTRAL ODONTOGENIC FIBROMA WITH ASSOCIATED CENTRAL GIANT CELL GRANULOMA (COLLISION TUMOR?) REPORT OF 7 CASES . S. Hassan, R. Reich, P. Freedman NY Hospital Queens, NY In 1992 Allen et. al were the first to report three cases of Central Odontogenic Fibroma (COF) with an associated giant cell reaction. The lesions were interpreted as COF - WHO type in which the giant cell component was reactive. Nine more cases have been reported. The etiology of this lesion is unknown but it has been theorized that it may represent a collision tumor. Therefore, the term Collision Tumor has been proposed. We present seven additional COF ,s with associated Central Giant Cell Granulomas (CGCG) [Collision Tumor] . All of our cases occurred in the mandible. A strong male predilection (5:2 M: F) was noted and the average age was 49 years. Three of the seven cases recurred (43%). Interestingly, one case recurred solely as a central giant cell granuloma. Immunohistochemical stains for AE1/AE3 and CK 19 were performed on the case that recurred as a central giant cell granuloma but did not reveal any odontogenic rests. In our series we note a higher recurrence rate than previously identified and a strong predilection for the mandible. No patient demonstrated any evidence of hyperparathyroidism. Because of the recurrence of one lesion as only a CGCG, we explore the possibility that these lesions do represent true collision tumors and not a reactive phenomenon.

Oral Abstracts – *Tuesday, June 24*

#9 - Time presenting: 16:06 – Venetian Room (Lobby Level)

GRANULOMATOUS FOREIGN-BODY REACTION INVOLVING THE ORAL AND PERIORAL TISSUES AFTER INJECTION OF BIOMATERIALS: A SERIES OF SEVEN CASES AND REVIEW OF THE LITERATURE. B.C. Jham, N. G. Nikitakis, M. A. Scheper, J. C. Papadimitriou, B. A. Levy, H. Rivera. U. Maryland, Baltimore, National and Kapodistrian U of Athens, Greece, and Central U. of Venezuela, Caracas. Objective: Injectable implants used for soft tissue augmentation may lead to a granulomatous foreign-body reaction. The aim of this report is to present seven new cases of foreign-body granulomas involving the oral and perioral tissues, after injection of biomaterials to achieve soft tissue augmentation. In addition, the clinical and epidemiological profile of this condition is summarized based on a comprehensive review of the English literature of all previously described cases. Findings: The literature search revealed 49 cases of this condition affecting the oral and perioral tissues. Our seven patients were female, with a mean age of 52.8 years (range 34-70). The lower lip was affected in four cases; one case was located in the upper lip, one case in the buccal mucosa, while one case involved two different sites (upper lip and buccal mucosa). Histopathologic examination revealed numerous cells with clear, often multiple, cytoplasmic vacuoles, bearing resemblance to lipoblasts. Immunohistochemistry revealed diffuse positivity for CD68. Conclusions: The diagnosis of granulomatous foreign-body reactions may be challenging, due to their microscopic resemblance to liposarcomas, and the occasional reluctance of the patients to report the previously performed esthetic procedure. Clinical history, histopathologic examination and, when needed, immunohistochemical analysis are essential to achieve accurate diagnosis.

#10 - Time presenting: 16:18 – Venetian Room (Lobby Level)

FIBROBLASTS IN ARECANUT CHEWERS. D.G.Mathew, N. Mahalakshmi, R.Sudharasana, R.Gunaseelan, K.Ranganathan Ragas Dental College and Chennai Dental Research Foundation, Chennai OBJECTIVE: The study was done to characterize fibroblasts from the buccal mucosa of areca nut chewers with and without clinical oral submucous fibrosis (OSF) by determining a) the ratios between fibroblast phenotypes b) cell cycle status and c) growth curve derivatives. METHOD: Fibroblasts were cultured from buccal mucosa of clinically asymptomatic areca nut chewers, areca nut chewers with OSF and normal subjects without habits (n=3 each) by collagenase disaggregation method. Cell lines from 4th to 6th subcultures were used for the study. RESULTS: Seven phenotypes were identified (F1-F7). A significant increase was found in the F3 and post-mitotic fibroblast subpopulations in comparison to mitotic subpopulations in chewers with and without OSF when compared to control group. A significant increase in the mean percentage of dead cells, a prolonged population doubling time and multinucleated giant cells were seen in areca nut chewers with OSF. We observed variants of F2 subpopulation among all the 3 groups. CONCLUSION: The altered phenotypes indicate that pathologic alterations occur early in chewers and cellular alterations are present even when the areca nut chewers are asymptomatic

Oral Abstracts – *Tuesday, June 24*

#11 - Time presenting: 16:30 – Venetian Room (Lobby Level)

PRIMARY DIFFUSE LARGE B CELL LYMPHOMAS OF THE ORAL CAVITY: GERMINAL CENTER CLASSIFICATION. H. Chhatwal, D.M. Cohen, S.Z. Al-Quran, I. Bhattacharyya. U. of Florida, Gainesville. Diffuse large B-cell lymphoma (DBCL) are the most common lymphoid malignancy. In the past classification of DBCL based on cytological variation has been proposed but no significant difference in survival has been found in these groups. In addition, the differentiation appears subjective. Recently, several reports have highlighted the value of dividing DBCL into prognostically important subgroups namely, germinal center B-cell like (GCB) and non germinal center B-cell like (non-GCB) lymphomas. GCB lymphomas have a much better prognosis than non-GCB lymphomas. Studies validating the above classification have been done for tumors of the breast, CNS and GI tract. Therefore, we undertook this study to examine if primary oral DBCL reflect this trend. We identified 9 cases diagnosed as DBCL from our archives dating from 2003-2007. Immunohistochemistry (IHC) was performed using antibodies against germinal center markers (CD10, bcl-6), activated B-cell markers (MUM1, bcl-2) and Ki-67 (proliferation marker). Cases were classified as GCB subgroup if CD10 and/or bcl-6+ and MUM1 \ominus , and as non-GCB subgroup if CD10 \ominus and MUM1+. Of the 9 cases, the age range was 38 to 91 years. Immunoreactivity was noted in 2/9 cases for CD10, 8/9 for bcl-6, 5/9 for MUM1, and 4/9 for bcl-2. Thus, 5 cases (55.56%) were classified in the non-GCB subgroup, and 4 cases (44.44%) in the GCB subgroup. All tumors showed frequent labeling with Ki-67 (60-90%). Our analysis showed, primary oral DBCL have an almost equal distribution of the two subgroups. Both subgroups show high proliferative activity and frequently express bcl-2, an adverse marker in non-GCB DBCL. These findings could allow pathologists to provide a more accurate insight into the potential aggressive behavior and poorer prognosis exhibited by these lymphomas.

#12 - Time presenting: 16:42 – Venetian Room (Lobby Level)

HAY WELLS SYNDROME. H. Sedano University of California Los Angeles. Hay Wells eponym is used to refer to a rare form of ectodermal dysplasia inherited as an autosomal dominant due to mutation in the tumor suppressor gene p63 that maps to the long arm of chromosome 3. The main clinical manifestations are: ankyloblepharon, marked alopecia, erosive scalp dermatitis, nail dysgenesis, cleft lip and/or palate, alterations in teeth composition and morphology and several other abnormalities. Fraternal twins affected with this syndrome will be presented, their oral manifestations as well as other clinical findings will be discussed. A differential diagnosis with other forms of ectodermal dysplasia will be established. The clinical manifestations of various syndromes also due to mutations in p63 will be discussed.

Oral Abstracts – *Tuesday, June 24*

#13 - Time presenting: 14:30 – Vanderbilt Room (Terrace Level)

EXPRESSION OF CALRETININ ON UNICYSTIC AMELOBLASTOMA, ODONTOGENIC KERATOCYST, DENTIGEROUS CYST AND ODONTOGENIC ADENOMATOID TUMOR: IMMUNOHISTOCHEMICAL ANALYSIS WITH 3 DIFFERENT CLONES. D. Dozal, M. Nava, B. Aldape, F. García, F. Ocampo. Universidad Nacional Autónoma de México, Instituto Nacional de Pediatría, Universidad Autónoma de Baja California; México. The differential diagnosis among odontogenic cystic lesions can be problematic due to several reasons; mainly because of the absence of histological classical features. The immunohistochemical expression of proteins as calretinin can help to solve this problem. Calretinin is a calcium-binding protein with a possible role in enamel formation. Methods: 38 cases were studied, 9 cases of ameloblastoma unicystic (AU), 20 of odontogenic keratocysts (OKC), 8 of dentigerous cysts(DC) and 1 of odontogenic adenomatoid tumor (TOA). Three tissue microarrays were performed and immunohistochemically stained with calretinin antiserum (BioSB, Dako and Zymed). Results: TOA was negative to calretinin. Cytoplasmic calretinin (BioSB) expression was detected in 9/9 AU cases with a moderate intensity, 2/8 DC cases with a weak intensity; none of the OKC was positive. Cytoplasmic calretinin (Dako) expression was detected in 9/9 AU cases with a high intensity, 1/8DC and 1/20OKC, these last two cases with a weak intensity. Cytoplasmic calretinin (Zymed) expression was detected in 9/9 AU cases with a moderate intensity, 3/8DC with a weak intensity and 1/20 OKC with a moderate intensity. Conclusions: The expression of the antibody to calretinin is sensitive in the ameloblastic epithelium of the AUs, suggesting its use as a differential immunohistochemical marker among odontogenic cystic lesions. But, there are differences in intensity and pattern of reaction, as well as in the proportion of positive cells, this pattern might be linked to the disrupted specificity of the antibody by the detection system or laboratory production.

#14 - Time presenting: 14:42 – Vanderbilt Room (Terrace Level)

IMPACT OF CANDIDA ALBICANS ON β -DEFENSIN EXPRESSION TN ORAL CARCINOMA. L. Compton, S. Joly, R. Srikantha, Z. Kurago, and J.M. Guthmiller. University of Iowa, Iowa City, New York University, University of North Carolina, Chapel Hill. Human beta defensins (HBDs) are cationic antimicrobial peptides produced by epithelial cells in the oral cavity. Recently, we reported a β -defensin deficiency in oral cancer vs. normal cell lines (Compton et al., 2006). It has been suggested that cancerous tissues have an increased susceptibility for *Candida albicans* colonization and a reduced HBD-2 production in oral squamous cell carcinoma (OSCC) in response to *C. albicans*. Objectives: Our goal was to compare HBD-1, 2, and 3 expression in cancer and normal keratinocyte cell lines co-cultured with *C. albicans* as opposed to basal expression. Methods: 2 human OSCC cell lines and 2 primary gingival keratinocyte control cell lines were co-cultured for 24 hours with 3 *C. albicans* strains (FC5, FC 16, and FC20) at 102, 104, and 106 cells/ml. Total RNA was extracted and expression of HBDs were quantitatively assessed by Real-Time PCR. Results: Basal level of expression of the cell cultures for all three HBDs were significantly lower in cancer cell lines ($P < 0.05$); HBD-2 expression was absent in the cancer lines. HBD-1 and 3 expression was significantly induced in SCCI9 when co-cultured with *C. albicans* at 104 cells/ml ($P = 0.001$ and 0.0023 respectively). However, the amount of expression was still significantly less than basal expression observed for control cell lines ($P = 0.0037$). *C. albicans* adhesion varied in function of the cell line but did not correlate with the strain, inoculum, or level of HBD expression. Conclusions: Our results suggest that cancer cell lines may display an altered defensin expression in response to co-infection with *C. albicans*. These results corroborate the hypothesis that microorganisms may influence cancer progression.

Oral Abstracts – *Tuesday, June 24*

#15 - Time presenting: 14:54 – Vanderbilt Room (Terrace Level)

DENDRITIC CELLS (DC), GRAM-POSITIVE (G+) AND GRAM-NEGATIVE (G-) BACTERIAL PRODUCTS AS POTENTIAL CONTRIBUTORS TO ORAL SQUAMOUS CELL CARCINOMA (OSCC) PROGRESSION. Z. Kurago, L. Ramanthapuram, A. Lam-ubol. NYU, New York. Background: OSCC were reported to be colonized by G+ and G- bacteria and our own and other studies show that most OSCC typically contain numerous monocytes, macrophages and DC. Previously, we showed that interleukin (IL)-6 and other factors strongly associated with disease progression, are induced in monocyte-OSCC-lipopolysaccharide (LPS) co-cultures, leading to rapid activation of an important pro-survival factor signal transducer and activator of transcription (STAT)3, while OSCC cells alone vary significantly in the ability to make such factors. As DC likely contribute to mucosal homeostasis, we hypothesized that during DC-OSCC interactions, bacterial products are necessary to induce pro-survival inflammatory products. Results: Extensive in vitro studies of monocyte-derived DC, OSCC cell lines and OSCC specimens were first performed to validate this approach. We tested highly pure bacterial products lipopeptide (G+) and LPS (G-) and show that relative to OSCC cells alone, constitutive output of inflammatory products in OSCC-DC co-cultures was decreased, but G+ and G- products induced dramatic increases particularly in IL-6 and IL-8. These increases were due to the combined effects of bacterial products on DC and on OSCC cells, and OSCC cells express toll-like receptors for G+ and G- products. Conclusions: OSCC-DC interactions in the absence of bacteria may dampen the production of inflammatory mediators, while bacteria can induce pro-survival inflammatory products that have the potential to support cancer progression. The contribution of toll-like receptor activation in OSCC cells to promotion of carcinogenesis is under investigation.

#16 - Time presenting: 15:06 – Vanderbilt Room (Terrace Level)

IN VITRO EVALUATION OF PTEN, AKT, MDM2 AND P53 IN HEAD AND NECK SQUAMOUS CARCINOMA CELL LINES TREATED WITH EGF AND 17 AAG. F. Pontes, H.R. Pontes, F.Nunes and D.S. Pinto Jr. School of Dentistry, University of São Paulo, Brazil. Head and neck squamous cell carcinoma (HNSCC) represents 90% of all head and neck malignancies. Cancer growth, invasion and metastasis are due to several signaling pathways that, unfortunately, are not completely understood. The aim of this study was to evaluate the crosstalk between PTEN, Akt, Mdm2 and p53 signaling pathways in four different HNSCC cell lines (HN6, HN19, HN30 and HN31) and HaCat cell line (immortalized keratinocytes), treated with 10ng/ml EGF (epidermal growth factor) and 2 μ M 17-AAG. Western blot and immunofluorescence were performed in order to analyze PI3K/Akt signaling key target proteins: PTEN, Akt, Mdm2 and p53. Treatment of HNSCC cell lines with EGF resulted in activation of the PI3K/Akt pathway and enhanced cell proliferation. Results showed higher proliferative activity in HN31 cell line. Treatment of HNSCC cell lines with 17-AAG inhibits the proliferation in various levels. HN31 cell lines expressed PTEN and p53 in high levels and low expression for Akt and Mdm2 proteins. These findings suggest that 17-AAG could induce p53-dependent apoptosis in HN31 cell lines. In contrast, HN6 and HN19 cell lines displayed high levels of Akt and Mdm2 proteins resulting in decreased apoptosis and increased aggressive potential.

Oral Abstracts – *Tuesday, June 24*

#17 - Time presenting: 15:18 – Vanderbilt Room (Terrace Level)

DYSREGULATED EXPRESSION OF HOX GENES IN ORAL SQUAMOUS CELL CARCINOMAS. CC Bitu, MFS Destro, MA Lopes, J Jorge Junior, E Graner, RD Coletta. School of Dentistry, State University of Campinas, Brazil. Homeobox genes, specifically the HOX family, play an important role in the development by controlling cellular proliferation, differentiation and apoptosis. Expression of HOX genes is associated with many cancers including those of the prostate, ovary, kidney, lung, skin and leukemia. The aim of this study was to compare the expression levels of HOX genes between normal oral mucosa and oral squamous cell carcinoma (OSCC). Normal oral mucosa and oral SCC obtained from the same patient, and normal oral mucosa from patients without history of exposition to risk factors related to OSCC (smoking habit and alcohol consumption) were analyzed by semi-quantitative reverse transcriptase-polymerase chain reaction (RT-PCR) duplex method with specific primers for the control gene GAPDH and for each of the HOX members. Our results demonstrated that none of the normal oral mucosa samples from patients without risk factors related to OSCC expressed HOXA3, A5, A6, A7, A9, A10, A11, A13, B1, B3, B5, B8, B12, C12, D3, D4 and D12. The expression of HOXA4, A5, A7, A10, B7, C4, C5, C6, C8, C9, C10, C11, D9, D10, D11 and D13 was statistically higher in OSCC samples when compared with those from normal oral mucosa, regardless of risk factor association. The results of our study suggest that a dysregulated expression of specific members of the HOX family of homeobox genes may be related to the tumorigenesis and/or tumor progression of OSCCs. Supported by CNPq and FAPESP.

#18 - Time presenting: 15:30 – Vanderbilt Room (Terrace Level)

Intracellular mechanism of cell death induced by photosensitizer distribution in photodynamic therapy. WonBong Lim¹, HongRan Choi¹, JiEun Kim², SungGa Lee¹, InAe Kim¹, JinAn Jeong², JongWoon Song³, SunYeol You³, OkJoon Kim¹ ¹Department of Oral Pathology, 2nd stage of brain Korea 21 for School of Dentistry, Dental Science Research Institute, Chonnam National University, Bug-Gu, Gwangju, 500-757, Korea ² K&C Welbeing Co. 116-11 NamDong, Dong-Gu, Gwangju, Korea ³ Department of oral and maxillofacial surgery, 2nd stage of brain Korea 21 for School of Dentistry, Dental Science Research Institute, Chonnam National University, Bug-Gu, Gwangju, 500-757, Korea. Photodynamic therapy (PDT) is based on specific photosensitizer accumulation in tumor tissue, followed by irradiation with visible light, which increases intracellular reactive oxygen species (ROS) and resulted in tumor cell death. However, the distribution of photosensitizers in target cells and their ROS induction to evoke cell death are not well understood yet. The present study is to carried out the PDT in KB cell line, oral cancer cell line, using a photosensitizer, Photofrin with 621nm irradiation. Confocal microscopy revealed that Photofrin was localized from cell membrane, cytoplasm to nucleus as the time went. In DNA fragmentation assay, necrosis was identified within 24 hours but apoptosis thereafter. The quantities of intracellular ROS was associated with the time of Photofrin accumulation. Additionally, western blotting analysis of Bcl-2/Bax, release of cytochrome C and caspase activities of caspase-3, and -9 showed that apoptosis followed mitochondrial dependent pathway. Taken together, PDT with Photofrin in KB cell line showed morphological changes of cell necrosis and apoptosis, which were associated with the time of distribution and/or localization of Photofrin. Also, the evoked apoptosis followed mitochondrial dependent pathway.

Oral Abstracts – *Tuesday, June 24*

#19 - Time presenting: 15:42 – Vanderbilt Room (Terrace Level)

METALLOTHIONEIN EXPRESSION IS ASSOCIATED TO METASTATIC BEHAVIOR OF ADENOID CYSTIC CARCINOMA OF THE SALIVARY GLANDS. M. T. Brazão-Silva¹, S. V. Cardoso¹, K. C. N. Souza¹, P. R. Faria¹, A. L. A. Eisenberg², M. F. Nascimento², F. L. Dias², A. M. Loyola¹. 1. Federal U. Uberlândia. 2. National Institute of Cancer - Brazil. In order to evaluate metallothionein (MT) as a predictive marker for metastasis development in adenoid cystic carcinoma of the salivary glands (ACC), we detected this protein by streptavidin-biotin-peroxidase immunohistochemistry in samples of this tumor: 37 primary non-metastasizing (PNM), 9 primary metastasizing (PM), and 2 metastasis (M). MT staining was observed in all of the samples. Nuclear positivity was a prominent feature in many lesions, while cells with ductal differentiation were usually negative. Semiquantitative analysis was performed by two observers to assess pattern (nuclear or cytoplasmic) of expression, intensity of staining, proportion of positive cells, and proportion of nuclear positivity. Inter-rater reliability was found moderate to good with this procedure. All of the obtained values for MT staining were constantly higher in PM than PNM cases. Mean intensity of staining was significantly higher in PM rather than PNM tumors. Distinct cut-off values could be traced to segregate only PNM cases. MT overexpression has been associated by other authors to poor prognosis in many malignant neoplasms. This protein is also associated with myoepithelial differentiation in salivary gland tumors and was found by us in a previous sample to be underexpressed in tubular rather than cribriform and solid subtypes of ACC. The results of the present study suggest that MT is also associated to the biological behavior of this salivary gland tumor. Therefore, this protein should be subject of further investigations to elucidate its participation in the development of ACC.

#20 - Time presenting: 15:54 – Vanderbilt Room (Terrace Level)

ROLE OF SALIVARY pH IN PATHOGENESIS OF OSMF. M. Donoghue, G.S.Madhushankari, P.Yadav and A.Gowda. College of Dental Sciences, Davangere, Karnataka. India. Arecanut & lime (CaOH) which are important components of pan/pan masala are both highly alkaline. Matrix Metalloproteinas (MMPs) responsible for degradation of extracellular matrix components such as collagen are highly sensitive to surrounding pH. The objective of this study is to investigate the role of rise in salivary PH and its subsequent delay in returning to base levels in pathogenesis of OSMF. Methods: Study is designed to examine a total of 60 individuals with the pan /panmasala chewing habits. The groups were designed to consist of equal numbers of subjects with and without manifestations of OSMF. Base line pH, pH after chewing pan/pan masala for 2 minutes and time taken for return to baseline PH are tested. Findings: preliminary results show significant differences in all values between subjects with and without the OSMF. Subjects with OSMF show a significantly higher salivary pH after chewing pan and their saliva takes a longer time to return to base line levels after chewing, while subjects who have had the habit of pan/panmasala chewing for longer than ten years and have not developed OSMF show lower increase in pH immediately after chewing pan/pan masala and a faster return to base line pH. Conclusions: from the findings of this study we conclude that salivary pH and buffering capacity for alkaline challenge play an important role in pathogenesis of OSMF in subjects who habitually use areca nut in different forms.

Oral Abstracts – *Tuesday, June 24*

#21 - Time presenting: 16:06 – Vanderbilt Room (Terrace Level)

PROLIFERATIVE AND APOPTOTIC MARKERS IN ORAL SUBMUCOUS FIBROSIS(OSF).K. Ranganathan, R. Kavitha. Ragas Dental College, Chennai. Background: OSF is a chronic, progressive premalignant condition of the oral mucosa, associated with areca nut chewing. Very little data of proliferative and apoptotic markers exists for OSF. Objective: To assess p53, Ki67, Bax and Bcl-2 expression in OSF (n=50), normal (n=10) and Oral cancer (n=10). Method: Immunohistochemical staining on sections from paraffin embedded tissues. Assessment and analysis of intensity of staining and labeling index (LI) was done using Pro series capture kit and software (Media cybernetics) and BX51 Olympus microscope with single chip CCD. Data were analyzed using SPSS v10.0.5. Kruskal-Wallis and chi-square test were applied appropriately. Results: Significant differences in the staining pattern were seen for p53, Ki67 and Bax for all three groups. Mean LI of p53 and Ki67 was significantly higher in OSF and cancer than in normal (p=0.00). Bax staining also showed significant differences in the intensity of staining between the three groups (p=0.00). Conclusions: Proliferative and apoptotic markers have potential to be used as surrogate markers in evaluation of OSF.

#22 - Time presenting: 16:18 – Vanderbilt Room (Terrace Level)

DETECTION OF POLYMORPHISM IN PROMOTER REGION OF MMP3 GENE AS A RISK FACTOR IN PATHOGENESIS OF ORAL SUB MUCOUS FIBROSIS AND ORAL SQUAMOUS CELL CARCINOMA- A MOLECULAR GENETIC STUDY. V.K. Hazarey P. Zade, S. R. Gosavi, S.M. Ganvir. Department of Oral Pathology and Microbiology, Government Dental College and Hospital Nagpur, Maharashtra, India. Among MMP family, MMP3 (stromelysin 1) is crucial in connective tissue remodeling as it can degrade types II, IV, IX and X collagens, extra cellular matrices as well as activate other MMPs. Promoter regions are specific segments of DNA that control the rate of mRNA synthesis. Thus, polymorphism in (5A/6A) promoter region of MMP3 gene results in different transcriptional activities. The promoter polymorphism of MMP3 has been related to susceptibility in some diseases. Genomic DNA obtained from blood of OSF (n=20), OSCC (n=20) normal individuals with tobacco habit (n=20), and without habit (n=20), were subjected to polymerase chain reaction of MMP3 gene promoter region followed by DNA sequencing of five randomly selected samples from each group. Results: The 5A genotype in MMP3 promoter region was observed more frequently in OSF group(4/5) than control groups(0/5). No significant difference was noted between OSCC(1/5) & control groups(0/5) on the 5A genotype. Controls(5/5) and OSCC(4/5) showed 6A Genotype. The results indicate that 5A genotype of MMP3 promoter region was associated as a risk factor of OSF but not OSCC.

Oral Abstracts – *Tuesday, June 24*

#23 - Time presenting: 16:30 – Vanderbilt Room (Terrace Level)

PHYSIOTHERAPEUTIC TREATMENT IMPROVES ORAL OPENING IN ORAL SUBMUCOUS FIBROSIS. S Cox, H Zoellner Oral Pathology and Oral Medicine, The Faculty of Dentistry, The University of Sydney, Westmead Centre for Oral Health. Westmead, NSW 2145, Australia. In oral submucous fibrosis (OSF) fibrous bands and burning mucosal pain restrict oral opening which limits speech and eating. The pathogenesis of OSF remains unclear. Surgical and pharmacological treatments have limited success and are often not accessible in communities using areca nut where OSF is prevalent. Improved outcomes are reported for surgical treatment when followed by physiotherapy. We tested the hypothesis that physiotherapy alone can modify tissue remodelling in OSF to increase oral opening. Fifty-four Nepali patients diagnosed with OSF were managed for 4 months. They were randomly assigned to three groups. Group 1 (23 patients) received 5 times daily physiotherapy by inter-positioning tongue spatulas between teeth and adding a new spatula every 5 to 10 days; Group 2 (15 patients) received local injection of hyaluronidase with steroids and Group 3 (16 patients) had no active treatment. More males were diagnosed with OSF than females ($p < 0.05$). All patients reported reduced opening and 47% had mucosal pain. Progressive mucosal involvement was always in the same order, starting with the soft palate, and then progressing to the fauces, unilateral buccal mucosa, bilateral buccal mucosa, floor of mouth and finally lip mucosa ($p < 0.006$). Physiotherapy improved oral opening ($p < 0.0005$), but not oral pain. No improvement was documented in the patients managed by injection nor in patients from the untreated group. We conclude that OSF in the Nepali population progresses in a predictable pattern, and that physiotherapy is an effective method of increasing their mouth opening. We further suggest that physiotherapy can be readily used to improve OSF in communities with otherwise limited health resources.

#24 - Time presenting: 16:42 – Vanderbilt Room (Terrace Level)

SOMATIC MUTATIONS IN C-KIT, NRAS AND BRAF IN ORAL MUCOSAL MELANOMA. R. Rivera, H. Nagatsuka, M. Gunduz, C. Siar, B. Cengiz, M. Fujii, Kok Han Ng and N. Nagai. Okayama U, Japan. Oral mucosal melanoma (OMM) is an aggressive tumor with a poor prognosis. Somatic events leading to activating mutations in certain proto-oncogenes may occur during melanomagenesis. C-kit is a trans-membrane receptor tyrosine kinase expressed during melanocyte development. Gain-of-function mutation in c-kit drives oncogenesis activating the RAS-RAF-MEK-ERK-MAPK pathway and mutation in RAS may also activate the PI3K-AKT pathway, which will eventually lead to cellular proliferation and inhibition of apoptosis. The objectives of the study were to determine the incidence of mutation in c-kit, NRAS and BRAF as well as the protein expressions of c-kit and RAS in OMM. Mutation analysis and immunohistochemistry were performed using 18 cases of human primary OMM. C-kit and RAS protein expressions were observed in OMM. Atypical melanocytes specifically expressed c-kit. C-kit expression was observed in both in situ and invasive components. OMM cases harbored c-kit, NRAS and BRAF mutations and the highest incidence of mutant alleles were found in c-kit. C-kit mutated cases were independent from cases with NRAS and BRAF mutations. On the contrary, NRAS and BRAF mutations were both found in one case. Incidentally, two c-kit mutations coincided with intense protein expression in the invasive component. C-kit expression in atypical melanocytes suggests its role in the early stage of OMM tumorigenesis. Somatic mutations in NRAS and BRAF are not common but probable events in OMM tumorigenesis. C-kit mutation may be functionally equivalent to the crucial activation RAS-RAF-MEK-ERK-MAPK and PI3K-AKT pathway suggesting c-kitTMs pertinent role in the tumorigenesis of OMM. Insights on the genetic changes may lead to the development of pathway-specific therapies that may improve prognosis.

Oral Abstracts – *Tuesday, June 24*

#25 - Time presenting: 14:30 – Hunt Room (Mezzanine Level)

CONCURRENT HPV-ASSOCIATED TONSILLAR CARCINOMA IN TWO COUPLES

E. Andrews, T. Seaman and J. Webster-Cyriaque. UNC School of Dentistry, Chapel Hill, North Carolina
Background: Human papillomavirus (HPV), the primary etiological factor implicated in most cervical cancers, has led to the recent development of a HPV vaccine. Oral-genital contact has been shown epidemiologically to result in oral and cervical cancers within couples. Concurrent oral cancers in partners with close proximity have not previously been described. This report describes two couples, with no smoking or drinking history, who developed HPV associated tonsillar cancer within 12 months of each other. Methods: After histopathologic evaluation, DNA was extracted from biopsy tissue of both couple members. HPV presence was identified by amplification of the HPV L1, E6 and LCR regions, with subsequent sequence alignment and phylogenetic analysis of sequenced amplimers. A real time assay targeting the HPV16 and 18 L1 & E7 regions was performed. Results: Tissue samples from each couple member were positive for HPV-16, the most prevalent type found in other HPV-associated cancers. Sequence analysis of 3 HPV DNA regions from both couples showed distinct inter-couple nucleotide differences and multiple unique intra-couple similarities. Sequences were also phylogenetically unique when compared to other HPV + cancer samples. Conclusions: This report demonstrates, for the first time, detection of matching strains of HPV16 in two couples with concurrent development of tonsillar carcinoma in the absence of other risk factors, revealing the potential infectious nature of oropharyngeal cancer. HPV presence in tonsillar cancers suggests its similar role in transforming oral epithelium, providing further evidence of the need to vaccinate men and women.

#26 - Time presenting: 14:42 – Hunt Room (Mezzanine Level)

ABNORMAL DNA CONTENT IN ORAL EPITHELIAL DYSPLASIA CORRELATES WITH INCREASED RISK OF MALIGNANT PROGRESSION

G. Bradley, E. Odell, J. Ho, S. Benchimol and S. Kamel-Reid. Faculty of Dentistry, Ontario Cancer Institute, Sunnybrook Health Sciences Centre, U. of Toronto; York University, Toronto, Canada; KingTMs College London, United Kingdom. Oral epithelial dysplasia is a potentially malignant lesion, but currently there is no simple, reliable assay to indicate risk of progression. We hypothesize that genomic instability contributes towards cancer development, and thus abnormal DNA content can distinguish the dysplastic lesions that will progress to cancer. Objective: to analyze a series of oral dysplasias for DNA content and correlate with progression to carcinoma. Methods and Findings: all biopsies of dysplasia accessioned to the Oral Pathology Diagnostic Service, U. of Toronto from 1993 to 2002 were matched against records of oral carcinoma from 1993 to 2007 in the Ontario Cancer Registry. 101 of 1480 biopsies were associated with subsequent carcinoma at the same or a contiguous site after 6 to 131 months (median 39 months). The dysplasias that progressed included 29 mild dysplasias, 29 moderate, 35 severe and 8 carcinoma-in-situ, with no correlation between grade and interval to carcinoma. Nuclear DNA content was measured by image cytometry (Perceptronix, Vancouver, Canada) in 27 dysplasias that progressed and 25 that have not progressed after 61 to 150 months (median 91 months). 12 of 27 progressed cases had abnormal DNA content that could reflect tetraploidy or aneuploidy while 2 of 25 non-progressed cases showed these abnormalities ($p < 0.01\%$). Among tongue lesions, 8 of 11 progressed lesions had abnormal DNA content compared to 2 of 9 non-progressed lesions. Conclusions: genomic instability is frequently detectable in the pre-invasive stage of oral cancer and DNA content analysis is a simple assay that can indicate malignant potential in oral epithelial dysplasia.

Oral Abstracts – Tuesday, June 24

#27 - Time presenting: 14:54 – Hunt Room (Mezzanine Level)

QUANTITATIVE TISSUE PHENOTYPE: AN ADJUNCT TOOL FOR PATHOLOGISTS TO ASSESS CANCER RISK OF ORAL PREMALIGNANT LESIONS (OPL). L Zhang, M Guillaud, C Poh, C MacAulay, M Rosin. U of British Columbia, BC Cancer Research Centre, Vancouver. Rapid computer technology development is transforming our world. In a recent retrospective study, we explored the value of a computer-driven microscope imaging system as an adjunct tool to assist pathologists in judging the progression risk of OPLs with no or low-grade (mild/moderate) dysplasia (termed LGOPL). Histology is poor in judging the cancer risk of LG OPLs. The study determined a Nuclear Phenotypic Score (NPS) that best discriminate normal from cancer, and showed that elevated NPS was strongly associated with high-risk molecular pattern and cancer progression (Cancer Research, 2008 in press). Objective: to assess the potential of this new tool in identifying high-risk LGOPLs from an ongoing prospective study. Methods: 192 primary LGOPLs from 151 patients were studied: 34 hyperplasias, 86 mild and 72 moderate dysplasias. Thoinin-Feulgen stained sections were imaged and analyzed to generate a NPS for each sample. All samples were assayed LOH on 7 arms (3p, 9p, 4q, 8p, 11q, 13q, and 17p). The NPS was correlated with histopathology, LOH and progression to severe dysplasia, carcinoma in situ or invasive cancer. Results: Elevated NPS was significantly associated with high-risk molecular pattern and progression: high NPS was associated with 9.9-fold increase in risk of progression, and 3/122 (2%) with low NPS progressed as compared to 16/70 (23%) with high NPS ($P < 0.0001$). In the multivariate Cox model, LOH and NPS together were the strongest predictors for progression. Conclusions: These data support the potential utility of automated quantitative microscopy technology to assist pathologist in assessing progressing potential of low-grade OPLs (Supported by grant R01DE13124, NIDCR).

#28 - Time presenting: 15:06 – Hunt Room (Mezzanine Level)

PLOIDY IN ORAL CARCINOGENESIS. A. Hirshberg, T. Shani, N. Yarom, S. Taicher, A. Cahbba, I. Ben Dov, I. Kaplan, R. Yahalom, N. Amariglio, G. Rechavi, L. Trakhtenbrot. The Chaim Sheba Medical Center and the School of Dental Med, Tel-Aviv U, Israel. Chromosomal numerical aberrations are an early event in oral carcinogenesis. We aimed to develop a noninvasive method for early detection of aneuploid cells (ACs) obtained by oral brush samples from premalignant, malignant lesions and from heavy smokers. Results: The study group included 207 individuals; 100 heavy smokers, 57 oral lichen planus (OLP), 35 patients with oral leukoplakia and 15 with squamous cell carcinoma (SCC). 35 patients were selected as control group. Cells were obtained by use of a disposable brush and were simultaneously analyzed for morphology and FISH using a multiparametric cell scanning system. Dual FISH was performed using centromeric probes for chromosome 2 and 8. Two of the control subjects had less than 1.5% ACs in the examined samples. Over 2% of ACs was detected in all cases with SCC, in 45% of the leukoplakia cases, in 24% of patients with OLP and in 12% of the smokers. In leukoplakia, the proportion of ACs increased with the severity of the histopathologic diagnosis. Four patients, 2 with oral leukoplakia and 2 with OLP developed SCC; in these patients a significant proportion of the cells were aneuploid. Most of ACs had normal morphology. Conclusions: ACs can be detected in early stages of oral carcinogenesis, and in high risk patients with normal looking mucosa. We suggest that the supplement of a brush sample and the combined morphological and FISH analysis of the cells collected enable early detection of potentially malignant conditions and monitoring of high risk patients.

Oral Abstracts – *Tuesday, June 24*

#29 - Time presenting: 15:18 – Hunt Room (Mezzanine Level)

P16 METHYLATION PREDICTS MALIGNANT TRANSFORMATION IN ORAL EPITHELIAL DYSPLASIA. G Hall, R Shaw, J Woolgar, L Liloglou, J Risk. Molecular Genetics and Oncology Group, Dept of Dental Sciences, U of Liverpool, UK. Management of the patient with oral epithelial dysplasia (OED) depends on the ability to predict malignant transformation. Histological grading of OED often fails in this regard and is also subject to inter and intra-pathologist variability. This study uses longitudinal clinical samples to explore the prognostic value of a previously validated panel of methylation biomarkers in a cohort of patients with histologically proven OED. The methylation enrichment pyrosequencing (MEP) assays used offer the sensitivity of traditional methylation specific PCR (MSP) but benefit from the added specificity advantages of a subsequent confirmatory sequencing reaction. Validation by pyrosequencing thus allows the exclusion of all false positive results and also checks for adequacy of bisulphite conversion. Our data show that methylation of the p16 gene promoter predicted for malignant transformation (Fishers exact test $p=0.002$). 26% (26/100) of samples in 57% (8/14) of patients with a lesion that transformed to OSCC demonstrated p16 methylation. In those patients not undergoing malignant transformation within 3 years, only 1% (2/184) of samples in 8% of patients (2/24) had p16 methylation, both samples being the most recently collected with continuing clinical review. Promoter methylation in MGMT, CYGB and cyclin A1 did not correlated with malignant progression. This preliminary study demonstrates that promoter methylation of p16 is a promising biomarker in aiding prediction of malignant transformation of OED and also has therapeutic implications in terms of chemoprevention with topical de-methylating agents.

#30 - Time presenting: 15:30 – Hunt Room (Mezzanine Level)

A ROLE FOR DYSKERIN IN ACTIVE CELL PROLIFERATION. F. Alawi, P. Lin. U. of Pennsylvania, Philadelphia. Dyskerin (DKC1) is a key component of the telomerase complex and is required for normal telomere maintenance. DKC1 also plays a role in rRNA processing and is needed for ribosome biogenesis. Our recently published studies demonstrate that DKC1 expression is activated during cellular growth and proliferation. DKC1 is significantly upregulated in oral squamous cell carcinomas relative to patient-matched normal controls; and is also uniformly high in transformed cell lines. We now show that DKC1 levels are also elevated in exponentially-growing, primary and immortalized oral keratinocytes relative to their respective, senesced or contact-inhibited cells. Proteasome inhibitors are being tested in clinical trials for the treatment of various cancers, including those of the head and neck; inhibition of the proteasome leads to potent, caspase-dependent apoptosis. Thus, to further test the hypothesis that DKC1 is needed during active proliferation, we incubated SCC1 oral squamous carcinoma cells with the proteasome inhibitor, MG132. Within two hours after exposure, the SCC1 cells exhibited a G2 arrest with a concomitant decrease in DKC1 expression by more than 40% relative to controls. Moreover, the effects of MG132 on DKC1 may be independent of the latterTMs role in telomerase, as similar findings were observed in telomerase-positive SCC1 cells and the telomerase-negative U2OS human osteosarcoma cell line. The reduction in DKC1 expression was also not a consequence of diminished transcription or due to de novo translation of other factors that might promote rapid degradation of the protein. However, the observed effects were completely prevented through co-incubation with the pan-caspase inhibitor, QVD-OPH. In summary, our data indicate a role for DKC1 in active oral keratinocyte proliferation and identify DKC1 as a possible target of the apoptosis signaling cascade.

Oral Abstracts – *Tuesday, June 24*

#31 - Time presenting: 15:42 – Hunt Room (Mezzanine Level)

VEGF EXPRESSION BY HUMAN DYSPLASTIC OR MALIGNANT ORAL KERATINOCYTES MAY BE RELATED TO INCREASED MAST CELL DENSITY AND THE SUBSEQUENT ANGIOGENIC ACTIVITY

A.K. Markopoulos, E.Michailidou, D.Z. Antoniadis. Aristotle U. of Thessaloniki, Greece. AIM: The aim of the present study was to elucidate the role of vascular endothelial growth factor (VEGF) and mast cells in neoangiogenesis during the progression from normal oral tissue through oral dysplasia to oral squamous cell carcinoma (OSCC). MATERIALS AND METHODS: VEGF expression by oral keratinocytes and microvessel density (MVD) in the chorium were studied immunohistochemically using an anti-VEGF and an anti-CD34 antibody respectively and mast cell density (MCD) using a toluidine blue counterstaining in 51 tissue samples, 29 OSCCs, 17 oral leukoplakias, 4 without dysplasia, 4 with mild, 4 with moderate, 5 with severe dysplasia and 5 samples from normal oral tissue. RESULTS: A gradually increased VEGF expression by oral keratinocytes, MVD, MCD was found from normal oral tissue, leukoplakia without dysplasia, leukoplakia with dysplasia and OSCC. VEGF expression was found to be related to MCD but not to MVD whereas MCD was found to be related to MVD. CONCLUSIONS: During the progression from normal oral tissue to OSCC, mast cells seem to be attracted by the epithelial VEGF secretion to the lesion site and may be related to the increasing microvessel density.

#32 - Time presenting: 15:54 – Hunt Room (Mezzanine Level)

ORAL SQUAMOUS CELL CARCINOMA: TIGHT JUNCTION CLAUDIN-7 DOWNREGULATION IS IMPLICATED IN ADVANCED STAGES OF THE DISEASE

MMS Nico¹, C.M. Coutinho-Camillo², M.E.C. Buim², A.C. Carvalho², R.C. Lessa², C. Pereira², A.L. Carvalho², L.P. Kowalski², F.A. Soares^{1, 2}, S.V. Lourenço¹ ¹Department of General Pathology, Dental School, U. of São Paulo; ²Hospital A.C. Camargo, São Paulo (E Brazil). Claudins, a large family of essential tight junction (TJ) proteins are abnormally regulated in human carcinomas. These proteins may be potential targets for cancer detection and therapy. Previously, we detected altered claudins expression in oral squamous cell carcinoma (OSCC) and this was associated with their clinico-pathological features. The present work analyzed immunohistochemical expression of claudin-7 in a Tissue Microarray (TMA) of 133 OSCC. We have also studied the expression of claudin-7 mRNA transcripts and methylation status of the claudin-7 promoter region. Results: Claudin-7 was almost absent in the majority of the cases (90.9%). Loss of claudin-7 was associated with advanced stages of OSCC (p=0.044) and was more frequent in moderately/poorly differentiated tumors (p=0.055). Loss of claudin-7 was also associated with tumor depth higher than 3mm (p=0.020). Disease-free survival was significantly shorter in claudin-7 negative patients (p=0.015). Down-regulation of claudin-7 transcripts was detected in 77.78% of the cases analyzed. As methylation is one of the mechanisms involved in downregulation of claudins, the methylation status of the promoter region of claudin-7 was investigated. We found that treatment of O28 cells (that did not express claudin-7 mRNA transcripts) with 5-Aza-2'-Deoxycytidine (5 Aza dC) led to the re-expression of claudin-7 mRNA transcript. Conclusion: Loss of claudin-7 expression might be associated with the tumorigenic process of OSCC and it is associated with poor prognosis. Furthermore, claudin-7 downregulation is probably due to hypermethylation.

Oral Abstracts – *Tuesday, June 24*

#33 - Time presenting: 16:06 – Hunt Room (Mezzanine Level)

EGFR-TYROSINE KINASE INHIBITOR ZD1839 DOWNREGULATES CD147 AND EXTRACELLULAR MATRIX MOLECULES IN ORAL PREMALIGNANT CELLS. N. Vigneswaran, J. Wu, S. Thevananther, J. Bouquot and W. Zacharias. UTHSC-Houston, Baylor College of Medicine TX, and U. of Louisville KY. EGFR signaling plays a crucial role in oral squamous cell carcinoma (OSCC) progression and is currently being targeted for OSCC chemoprevention. EMMPRIN/CD147 is a transmembrane glycoprotein that mediates tumor-extracellular matrix interaction and thereby promotes tumor progression. We reported upregulation of CD147 in oral premalignant (OPM) lesions, mainly at the pre-invasive stage. Aim: To investigate the effects of ZD1839 on the expression of CD147 and related ECM molecules in OPM cells. Results: Treatment of OPM cells (Leuk1) with EGFR-ligand amphiregulin (AR) lead to dose-dependent increases in CD147 expression. Pretreatment of cells with ZD1839 blocked AR-mediated upregulation of CD147. Using tunicamycin as glycosylation inhibitor, we confirmed that ZD1839 inhibited CD147 transcription but not glycosylation. Caveolin-1, which is functionally linked to CD147 glycosylation, was not affected. AR treatment of OPM cells activated ERK, JNK and PI3K/AKT pathways; however, ZD1839 blocked only ERK activation. ERK inhibitor PD98059 also blocked AR-induced CD147 expression; thus, ERK signaling selectively mediates EGFR-linked CD147 up-regulation in OPM cells. ZD1839 significantly ($p < 0.01$) inhibited OPM cell migration and invasion, but had only a minimal inhibitory effect on OPM cell proliferation. RT2-Profiler™ PCR arrays (Super Array) showed that treatment of OPM cells with ZD1839 induced down-regulation of MMP-1, MMP-9, MMP-10, ADAMTS-1, integrin- α 2 and laminin- α 3, - β 1 and - β 3. Also, compensatory up-regulation of MMP-7 and MMP-13 was noted. Conclusion: ZD1839 inhibits OPM cell migration and invasion by blocking ERK activation, leading to down-regulation of CD147 and its functionally linked ECM molecules.

#34 - Time presenting: 16:18 – Hunt Room (Mezzanine Level)

IMMUNOHISTOCHEMICAL STUDY OF KI-67 AND MMP-1 IN PREMALIGNANT AND MALIGNANT ORAL LESIONS. Z. Mohamad Zaini, L. Pong, T. Lu, S. Cheong, A. Khanam, M. Jamaludin, and T. Abraham. Oral Cancer Research and Coordinating Centre, Malaya U., Kuala Lumpur, and Cancer Research Initiatives Foundation, Subang Jaya, Malaysia. In this study, we evaluated the proliferative and invasion potential occurred in dysplasia, oral lichen planus (OLP) and oral squamous cell carcinoma (OSCC). Retrospective studies of 87 formalin fixed paraffin embedded tissue specimens (30 dysplasia, 41 OLP and 16 OSCC) were cut out and put together using the Tissue MacroArray (TMaA) method to form a separate tissue specimen blocks prior to the staining with the proliferative (Ki-67) and the invasive (MMP-1) marker. The stained sections were scored for the mean average of positively stained cells using image analyser (Image Pro MDA-Media Cybernetics) version 6.1. One way ANOVA and Kruskal-Wallis test showed significant difference in mean number of positive cells for Ki-67 and MMP-1 antibodies respectively between dysplasia and OSCC, dysplasia and OLP and between OSCC and OLP. Pattern of expression of Ki-67 and MMP-1 were clearly differentiated between diagnostic categories suggesting that these markers maybe a useful indicator to look into the predictive aspect of malignant transformation of dysplasia and OLP in Malaysian population.

Oral Abstracts – Tuesday, June 24

#35 - Time presenting: 16:30 – Hunt Room (Mezzanine Level)

Free β -catenin in squamous cell carcinoma: Functional significance and role of rap1. M. Goto, R Mitra, M Liu, W Ao, and NJ D'Silva. U. of Michigan, Ann Arbor. Free β -catenin (β -cat), a central molecule in the Wnt signaling shuttles from the cytosol to the nucleus where, as a co-factor with T-cell factor/ lymphoid enhancer factor, it triggers the transcription of genes that promote tumorigenesis. β -cat's role in head and neck squamous cell carcinoma (HNSCC) is controversial. Furthermore, its mechanism of nuclear translocation is relatively unexplored. Rap1 is a ras-like protein that shuttles between the cytosol and nucleus in HNSCC. Our previous studies suggest that it has a role in nuclear transport of β -cat. The objectives of the current study were to investigate whether a) β -cat is linked to tumor progression in SCC; and b) whether nuclear translocation and functional effects of nuclear β -cat are blocked by RNAi-mediated downregulation of rap1. *Methods and Results.* Immunohistochemical studies on HNSCC cell lines, tissue sections and tissue microarrays showed that free and membrane-bound β -cat are present in HNSCC. Consistent with these findings, β -cat was detected in an E-cadherin binding assay for free β -cat. As reported previously, active rap1 binds to β -cat in SCC and HEK 293 cells. In 293 cells, rap1 upregulates β -cat dependent transcription via TCF4. To investigate the functional relevance of the rap1/ β -cat interaction, we measured invasion in HNSCC cells stably transfected with β -cat. Luciferase reporter gene assays showed that RNAi strategies to block rap1 downregulated transcription in HNSCC cells that overexpressed β -cat. Similarly, functional assays showed that RNAi-mediated knockdown of rap1 inhibited invasion of HNSCC cells overexpressing β -cat. *Conclusion and Significance.* Rap1-mediated nuclear translocation of β -cat induces transcription and invasion of HNSCC cells. This represents a potential therapeutic target in HNSCC. (This work was supported by NIDCR DE16920-01, DE018512-01 and NCI SPORE grant P50 CA97248.)

#36 - Time presenting: 16:42 – Hunt Room (Mezzanine Level)

RECONSTITUTION OF ORAL SQUAMOUS CELL CARCINOMA BY THREE IMMORTALIZED CELL LINES. Y.J. Park, D.P. Hong, Y.S. Hwang, C.M. Cha, B.K. Oh*, E.C Kim**, J. Kim. Oral Cancer Research Institute, Department of Oral Pathology, Yonsei Univ., Brain Korea 21 Project, Yonsei Cancer Center*, Wonkwang Univ.**, Korea. To study carcinogenesis of oral squamous cell carcinoma (OSCC), it is important to establish an in vitro multistep carcinogenesis model. Cell immortalization is considered to be a prerequisite status for cancer transformation. Accordingly, we established three kinds of immortalized cells and reconstituted OSCC in vitro. HPV16 E6/E7-induced immortalized human oral keratinocyte (IHOK: provided by EC Kim) was serially transfected with retroviral constructs containing hcdk4 and hcdk4/hTERT. Cell cycle related proteins were analyzed and telomerase activities were examined. Organotypic culture showed invasive OSCC in all three immortalized cell lines. Interestingly, in vivo tumorigenicity was found only in two cell lines, hcdk4 transfected-IHOK and hcdk4/hTERT-transfected IHOK. Three-dimensional in vitro model reconstituted by immortalized cells may be useful for further studies to investigate oral carcinogenesis. This study was supported by the Korea Research Foundation Grant funded by the Korean Government (MOEHRD), Basic research promotion fund (KRF-2005-005-05901).

Oral Abstracts – *Tuesday, June 24*

#37 - Time presenting: 14:30 – Garden Room (Lobby Level)

PROLIFERATION, APOPTOSIS, GROWTH FACTORS AND ONCOGENES IN AMELOBLASTOMAS. P.DeVilliers, H. Rivera, J. Santiago, M Rossi and M. Correnti. University of Alabama at Birmingham and Central University of Venezuela at Caracas.

Background: Ameloblastomas are aggressive epithelial tumors of odontogenic origin with high recurrence rate and local invasiveness. The purpose of the study was to evaluate the expression of proliferation and apoptotic molecules, epidermal growth factor, calretinin and oncogenes in Ameloblastomas. Design: A total of 18 ameloblastomas were selected, 11 of which, represented cystic ameloblastomas and 7 were solid/multicystic. Sections were obtained from formalin fixed, paraffin embedded tissue blocks and tested for epidermal growth factor (EGF), B cell/leukemia lymphoma 2 (Bcl2), protein 53 (p53), protein 21 (p21), Ki67 proliferation protein, proliferating cell nuclear antigen (PCNA) and calretinin (CAB 29) using immunoperoxidase techniques. Positive and negative controls were adequate. Results: All cases (100%) were immunoreactive for EGF at the basal layer and stellate reticulum-like area. PCNA was expressed in 15/18 (83%) at the basal layer; p53 was evidenced in 8/18 (44%) on both, the solid islands embedded within the connective tissue, as well as the basal layer of the unicystic types. Similar distribution was observed for p21 in 3/18 (17%) cases. Calretinin was observed in 4/18 (22%) predominantly at the stellate reticulum-like areas. Bcl2 and Ki67 were negative in all cases. Conclusions: EGF and PCNA were the most expressed markers in our series of ameloblastomas, indicating a high proliferation activity and therefore may influence tumor infiltration; the oncogenes tested could play a role in the transformation and differentiation of these tumors. Furthermore, our findings may contribute to the prediction of prognosis and clinical behavior. It is our intention to explore the role that EGF may play as a target for antitumor strategies.

#38 - Time presenting: 14:42 – Garden Room (Lobby Level)

HUMAN PAPILOMA VIRUS PRESENCE IN AMELOBLASTOMA. H Rivera, M Correnti, M Avila. Oral Pathology Laboratory. Central U. of Venezuela & Molecular Genetic Laboratory. Oncology and Hematology. Institute. Caracas, Venezuela

Ameloblastomas are benign epithelial tumors of odontogenic origin, with high recurrence rate and locally aggressiveness. Few preliminary studies have demonstrated the HPV presence mainly in peripheral ameloblastomas by in situ hybridization or PCR analysis. The aim of the present study was to detect HPV-DNA in intraosseous ameloblastomas. Eighteenth diagnosed cases of intraosseous ameloblastomas, different histological variants, from the files of the Oral Pathology Laboratory, Central University of Venezuela (2005-2008) were selected. Decalcified material was excluded from this study. The INNOLiPA HPV Genotyping v2 Amp kit, (Innogenetics, N.Y.) was used to amplify a part of the HPV L1 region using PCR technique. Of the 18 selected cases, seven were solid multicystic tumors (Follicular, Plexiform, Acanthomatous and Desmoplastic variants) and 11 were cystic. HPV-DNA was detected in 6/18 (33%) of the cases. HPV-6 was the most frequent genotype 4/6 (66%). The majority of the positive HPV-DNA cases corresponded to low oncogenic potential types. Only one case was HPV-DNA 11 and just one corresponded to high oncogenic potential (HPV-DNA 16,33). Interestingly, all positive HPV-DNA cases were cystic histological types. We may conclude that HPV positivity in the present study could be related to an infection derived from the dentigerous cysts epithelial lining since no solid variants were observed. Grant support : CDCH PG10-00-6522-2006 and FONACIT G-2005000408

Oral Abstracts – *Tuesday, June 24*

#39 - Time presenting: 14:54 – Garden Room (Lobby Level)

PTCH1 AND SMO GENE ALTERATIONS IN KERATOCYSTIC ODONTOGENIC TUMORS. T.-J. Li, L.-S. Sun, X.-F. Li. Peking U, Beijing, PR China. Keratocystic odontogenic tumors (KCOTs, previously known as odontogenic keratocysts) are aggressive jaw lesions that may occur in isolation or in association with nevoid basal cell carcinoma syndrome (NBCCS). Mutations in PTCH1 gene are responsible for NBCCS and are related in tumors associated with this syndrome. Mutations in SMO gene have been identified in basal cell carcinoma and in medulloblastoma, both of which are features of NBCCS. To clarify the role of PTCH1 and SMO in KCOTs, twenty sporadic and 10 NBCCS-associated KCOTs were examined for mutations of PTCH1 and SMO. Eleven novel (1 of which occurred twice) and 5 known PTCH1 mutations were identified. Interestingly, four patients (two sporadic, two syndromic KCOTs) harbored 2 coincident mutations respectively and one sporadic case appeared to have a mutant copy (c.403C>T) of PTCH1 while losing the normal copy, suggesting that a two-hit mechanism might occur in a subset of KCOTs. Additionally, we describe here an alternate splicing product of exon 10 skipping and 3 disease-associated aberrant splicing in PTCH1. By contrast, no pathogenic mutation was detected in SMO. Our findings suggest that mutations are rare in SMO but frequent in PTCH1 in sporadic and NBCCS-associated KCOTs.

#40 - Time presenting: 15:06 – Garden Room (Lobby Level)

DEVELOPMENTAL TOOTH DEFECTS AND SOFT TISSUE ABNORMALITIES IN PATIENTS WITH CRANIOFACIAL SYNDROMES.
G. S. Dalben, M. R. Gomide, A. Richieri-Costa, and L. A. A. Taveira. U. of São Paulo, Bauru, Brazil.
Objectives: Tooth abnormalities may be valuable diagnostic signs of syndromes and other diseases. Several studies have associated the genetics of tooth abnormalities and congenital malformations; such findings may enhance the understanding on the mechanisms underlying the development of tooth abnormalities and the occurrence of syndromes. Several studies are being conducted at our department to investigate the association between tooth abnormalities and soft tissue alterations and different craniofacial syndromes, including syndromic craniosynostosis, Treacher Collins syndrome, OAV spectrum, velocardiofacial syndrome and G/BBB syndrome. Findings: So far, these investigations revealed strong evidence of association between enamel opacities, tooth agenesis (especially of maxillary canines), ectopic eruption of maxillary first molars and lateral palatal swellings in individuals with syndromic craniosynostosis; enamel opacities, tooth agenesis and cleft lip and/or palate in patients with Treacher Collins syndrome; tooth agenesis in individuals with OAV spectrum, especially at the side affected by hemiatrophy; hypodevelopment of the lingual cusp of mandibular first premolars and enamel opacities in the velocardiofacial syndrome; and mandibular anterior supernumerary teeth and ankyloglossia in individuals with G/BBB syndrome. This presentation aims to present the methodology and detailed results of these studies, as well as preliminary findings of ongoing investigations on other craniofacial syndromes. Conclusions: Additional studies on different syndromes and employing molecular genetics techniques should be encouraged to further elucidate the common etiopathogenic factors causing both craniofacial syndromes and developmental tooth defects.

Oral Abstracts – *Tuesday, June 24*

#41 - Time presenting: 15:18 – Garden Room (Lobby Level)

BISPHOSPHONATE-RELATED OSTEONECROSIS- STAGING AND TREATMENT OUTCOMES OF 66 CASES. M. Lerman, N. Treister, S. Woo. Brigham and WomenTMs Hospital. Boston, MA. Background: Bisphosphonate-related osteonecrosis of the jaws (BRONJ) is characterized by exposure of necrotic jawbone after exposure to bisphosphonates. Objective: To describe a large series of cases of BRONJ with respect to staging and treatment outcomes following conservative management. Methods: Records of patients seen for BRONJ at the Division of Oral Medicine and Dentistry, Brigham and WomenTMs Hospital from January 2001 to January 2008 were reviewed. Patients were staged 0-3 according to standard criteria. All patients had a history of exposure to pamidronate, zoledronate, and/or alendronate. Results: There were 66 patients with underlying medical conditions including multiple myeloma (43), breast cancer (11), prostate cancer (6), lung cancer (3), osteoporosis (1), monoclonal gammopathy (1), and Gaucher disease (1). At initial visit, 50% were stage 1, 47% stage 2, and 3% stage 3. All were treated with systemic antibiotics, chlorhexidine gluconate, occasional localized debridements, and/or surgery. Of the patients with follow-up (n = 50), 23 (46%) had stable disease (12 stage 1, 11 stage 2), 26 (52%) underwent a decrease in stage, and one (2%) advanced from stage 1 to 2. Conclusion: Conservative management of BRONJ with chlorhexidine rinses, antibiotics and occasional localized debridements may be effective in keeping the majority of patients with stage 1 or 2 BRONJ from progressing.

#42 - Time presenting: 15:30 – Garden Room (Lobby Level)

MITF ISOFORMS IN OSTEOCLASTS. S. Lu, M. Li, and Y. Lin. U. of Kentucky, Lexington. Objectives: Osteoclast differentiation is regulated by a group of ubiquitous transcription factors that are present in many cell lineages. However, it is not clear how they are coordinated to regulate tissue-specific differentiation. Among these factors, Mitf is unique since mutations in the Mitf gene only affect specific cell lineages including osteoclasts. Two tissue-specific Mitf isoforms, Mitf-M and Mitf-Mc, have been identified in melanocytes and mast cells and are responsible for tissue-specific gene expression. We propose that Mitf also provides osteoclast-specific signals through an isoform that is osteoclast-specific or restricted. Findings: The results show that there are two abundant Mitf isoforms present in osteoclasts while there is only one in macrophages. Both isoforms have same functional domains but are different in their expression patterns, biochemical properties and osteoclastogenic activities. Conclusion: Osteoclast-restricted Mitf is the prime candidate linking the ubiquitous transcription factors to osteoclastogenesis.

Oral Abstracts – *Tuesday, June 24*

#43 - Time presenting: 15:42 – Garden Room (Lobby Level)

EFFECTS OF RANITIDINE ON RECURRENT APHTHOUS STOMATITIS - A PRELIMINARY REPORT.

Y-F Huang and H-W Yang. Chung Shan Medical University, Taichung, TAIWAN.

Recurrent aphthous stomatitis is a very common oral mucosal lesion which was characterized by repeated episodes of single or multiple ulcerations in the oral mucosa. Although the mechanism of the disease is still poorly understood, some indications have pointed to dysregulation of cell-mediated immune response. For severe cases, prednisolone is the first choice of treatment with an alternative by using cimetidine. Ranitidine is an H₂ receptor blocker mimicking cimetidine chemically. The purpose of this pilot study to test if ranitidine has therapeutic benefit on the treatment of recurrent aphthous stomatitis. A total of 20 cases (7 F, 13 M, ranging 18 to 58 y/o) were included in the study who have had recurrent aphthous stomatitis with a duration ranging 6 months to 20 years. All patients were treated with 30mg prednisolone per day for 7 days followed by a 3-month course of ranitidine (150 mg), bid. A 10-cm visual pain scale was used to assess the discomfort at the beginning and end of the treatment course. Among the 20 patients, 9 patients completed the 3-month treatment course at the time of abstract submission. The result showed the mean pain scale at the beginning of the study was 6.7 ± 1.9 , which was significantly reduced to 2.3 ± 1.6 at the end of the study ($p=0.000006$, student's *t*-test). This pilot study showed that ranitidine may be used to control recurrent aphthous stomatitis. A large scale, randomized, double-blinded clinical trial is needed for further study and is currently ongoing.

#44 - Time presenting: 15:54 – Garden Room (Lobby Level)

SHORT HELICAL PEPTIDE-1, MUCOCIDIN, A NOVEL ANTIMICROBIAL PEPTIDE GENE

EXPRESSED IN THE HUMAN MUCOSAL EPITHELIAL CELLS AND EXOCRINE GLANDS. Y. Kim, S.

Lee. Kangnung National U., Gangneung Korea. We identified a novel human gene encodes 46 amino acid antimicrobial peptide from the exocrine gland, designated as Mucocidin. Mucocidin is primarily expressed in mucosal epithelial cells and accessory secretory glands, and secreted into mucosal fluid and glandular secretions as an active mature peptide and associate with and crosslinked to epithelia to form the stable protective barrier or as an active free peptide. The full coding sequence of the 527 nucleotide cDNA expressed or synthetic peptide were bactericidal against *E. coli*. The peptide was also active against *S. aureus* and *C. albicans*.

Northern and mRNA array analysis of Mucocidin displayed wide expression in the diverse segments of mucosal cavity and exocrine gland epithelia. Identifying novel antimicrobial peptide Mucocidin and stable anchoring on the mucosal epithelium provided a new mechanism of protecting the mucosal tracts and play a key role in the innate immunity by enriching its distribution at the membrane.

Oral Abstracts – *Tuesday, June 24*

#45 - Time presenting: 16:06 – Garden Room (Lobby Level)

CORRELATIONS BETWEEN QUANTITATIVE PARAMETERS OF BACTERIAL COLONIES AND DISEASE COURSE IN ACTINOMYCES-ASSOCIATED LESIONS OF THE ORAL MUCOSA AND JAWBONES. I. Kaplan, K. Anavi, Y. Anavi, S. Calderon, A. Hirshberg. Rabin Medical Center and Tel-Aviv U, Israel. Objective: To correlate clinical course and treatment requirements with quantitative analysis of actinomyces (a.) colonies in biopsies from oral mucosa and jawbones. M&M: cases with microscopic evidence of a. were included. Actinomyces colonies were identified using Gram and PAS stains and the typical filamentous morphology, with variations in color between center and periphery. Only colonies with adjacent tissue reaction (inflammation, fibrosis) were analyzed. Using a 10X10 square grid objective, the total number and total surface of a. colonies, and total surface of the tissue were measured. A. density (AD) and a. relative surface (ARS) were calculated. Results: The study population included 110 cases (49 M, 61 F), age range 3-84 years, mean 49.8. They presented a wide clinical spectrum, involving jawbones and/ or oral soft tissues. Cases included osteomyelitis associated with bisphosphonate treatment, osteoradionecrosis, periapical lesions, odontogenic cysts, failing implants, periodontal disease, patients with compromised immunity and others. A linear correlation was demonstrated between mean AD and mean ARS, ($R=0.728$, $p<0.001$, Pearson). Both parameters correlated with the median length of antibiotic treatment. (AD: $R=0.292$, $p=0.006$; ARS: $R=0.238$, $p=0.028$). Conclusions: The results of the present retrospective analysis indicate that actinomyces-associated lesions are not rare, and that they present in a wide spectrum of clinical settings. Quantitative analysis of the number and surface of the bacterial colonies representing the bacterial load in the specimen could help in evaluating the aggressive potential of the lesion and help in treatment planning.

#46 - Time presenting: 16:18 – Garden Room (Lobby Level)

ORAL HAIRY LEUKOPLAKIA DIAGNOSIS BY IN SITU HYBRIDIZATION ON LIQUID BASED CYTOLOGY. M. Magalhães, R. Santos, K. Ortega, S. Pereira, P. Braz-Silva. Dental School, São Paulo U., and Adolfo Lutz Institute, SP, Brazil. Since the diagnosis of OHL has important clinical implications, it should be made at the definitive level, which requires the demonstration of EBV DNA in biopsies. The aim of this study was establish a non invasive and definitive diagnosis for OHL in exfoliative cytology samples. We studied 33 patients divided into 3 groups: G1, composed by 13 HIV+ patients with OHL diagnosed using gold standard criteria; G2 composed by 10 HIV+ patients with no OHL lesions, and G3 by 10 HIV negative patients with no lesions. For each patient a small brush was rotated to obtain lateral tongue epithelial cells. Thin layer DNA-Citoliq® system was used and EBV DNA detection was performed using in situ hybridization. EBV gene was detected in every specimen from G1 patients and in none patients from G2 and G3. We concluded that the brush biopsy technique is equivalent to surgical specimens in establish OHL diagnosis, with the advantages of safety, speed, cost and tolerability.

Oral Abstracts – *Tuesday, June 24*

#47 - Time presenting: 16:30 – Garden Room (Lobby Level)

IMMUNOHISTOCHEMICAL STUDY OF APO-1 RECEPTOR/LIGAND SYSTEM IN ORAL SQUAMOUS CELL CARCINOMA. R. Younis, H. Raslan, M. Warda, S Bastaweesy. U. Alexandria, Egypt. Apo-1/Fas is a transmembrane apoptotic receptor expressed in a variety of epithelial and immune system cells, upon binding to its ligand, it activates an apoptotic pathway. The Apo-1 ligand is expressed by activated T-lymphocytes, natural killer cells, plasma cells and immune privileged cells. This study aims to investigate how OSCC escape Apo-1 induced apoptosis. An immunohistochemical study of the Apo-1 receptor and ligand in twenty two primary oral squamous cell carcinomas (OSCC) was performed. In normal epithelium the receptor is expressed on the cell membrane of the basilar cells. This expression is lost in superficially invasive OSCC, which instead show retentive cytoplasmic staining. The peripheral cells of invasive OSCC tumor nests were negative for the Apo-1 receptor, while the central cells stained cytoplasmically. Staining intensity was greatest in well differentiated OSCCs, with a significant loss in poorly differentiated OSCCs ($p < 0.004$). The Apo-1 ligand was negative in the primary OSCCs cases. This study demonstrates the potential ability of OSCC to internalize the Apo-1 receptor and escape T-cell induced apoptosis. Thus, the expression pattern of the Apo-1 receptor can be considered as a prognostic marker for malignant progression.

#48 - Time presenting: 16:42 – Garden Room (Lobby Level)

EXPRESSION OF HSP70 IN THE MINOR SALIVARY GLANDS OF PATIENTS WITH SJÖGREN SYNDROME: AN IMMUNOHISTOCHEMICAL STUDY-PRELIMINARY DATA. E.Deligianni, A.K. Markopoulos, D.Z. Antoniadis. Aristotle U. of Thessaloniki, Greece. Heat shock proteins are expressed or increased in response to various biological stresses, with HSP70 as the major extracellular chaperone. Sjögren syndrome is an autoimmune disease of unknown etiology and its histological findings are characterized by the infiltration of inflammatory cells and the final destruction of salivary glands. Aim: The aim of this study is to demonstrate whether minor salivary glands in patients with Sjögren syndrome express HSP70 and also highlight the localization and degradation of this expression. Materials and Methods: Eighty paraffin embedded minor salivary glands, excised with the clinical implication of Sjögren syndrome and either confirmed or not with the diagnosis, are tested for HSP70 expression by means of immunohistochemistry. Results: In all cases an intense homogenous cytoplasmic staining is seen in both intercalated and striated ducts along with myoepithelial cells surrounding mucous acini. Discussion: According to our knowledge this study presents the first evidence that HSP70 is intensely expressed in minor salivary glands both in patients confirmed or not with the diagnosis of Sjögren syndrome.