549 and MDA-MB-468 cells at 17.2%, 14.8%, 13.2% and 14.9% respectively. To study their uptake capability, the labeled exosomes from different origins were incubated with a panel of breast cancer cells, including MCF-7, MDA-MB-231, MDA-MB-468 and BT-549, and normal NIH/3T3 fibroblast cells for 24 hours. The cells were then evaluated by fluorescence microscopic imaging and flow cytometry. It was observed that exosomes from different origins have a different uptake efficiency, suggesting that each exosome may have its unique navigation systems. Furthermore, the cells which have aggressive metastatic potential, such as MDA-MB-231 showed a better pickup of all exosomes. In contrast, the exosomes released by MDA- MB-468 showed higher loading in five kinds of cells.

Conclusions: Our development has demonstrated an effective labeling method that can facilitate exosome research by providing a new way of quantification and tracking in vitro and potentially in vivo studies.

THE CYTOSKELETAL ALTERATION MODULATES CELL INVASIVENESS OF OSCC CELLS THROUGH RHOA-YAP SIGNALING IN STROMAL FIBROBLASTS.

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Objectives: Cancer-associated fibroblasts (CAFs) are most abundant stromal cells among tumor microenvironment that participate in carcinogenesis. This study aimed to investigate the mechanism of cytoskeletal alteration of CAFs and its role in carcinogenesis of oral squamous cell carcinoma (OSCC).

Findings: We first evaluated if immortalized normal fibroblasts(hTERT-hNOFs) can be substituted for CAFs. hTERT- hNOFs co-cultured with OSCC cells showedmyofibroblastic and senescent phenotypeslike CAFs.Next, we observed the cytoskeletal alteration in hTERT-hNOFs co-cultured with OSCC cells, including enlarged cellular size, distinct F-actin assembly (stress fibers). To further understand the mechanisms, we identified the expression of RhoGT- Pase gene family. Among them, RhoA was significantly increased. These results were confirmed by RhoA-ROCK inhibitor(Y27632). In spite of fibroblasts grown with OSCC cells, Y27632 reduced cell size and stress fibers. Furthermore,YAP distribution, as a downstream transcriptional factor of RhoA, was examined. YAP was mainly localized at nucleus in hTERT-hNOF co-cultured with OSCC cells, unlike hTERT-hNOFs co-cultured with HEK(human normal epidermal keratinocyte). To further verify if RhoA and cytoskeletal change modulate YAP distribution, Actin polymerization inhibitor(Lat.A) and Y27632 were used. As results, the inhibitors interrupted nuclear YAP localization, suggesting that YAP can be regulated by RhoA-induced cytoskeletal alteration. Lastly, we examined if nuclear YAP localization of fibroblasts exacerbates OSCC progression. YAPS127A mutant fibroblasts, maintained in nuclear YAP, were generated. As results, YAPS127A showed cytoskeletal rearrangement, such as increased gel contractility and matrix stiffness, and thereby enhanced the invasiveness of OSCC cells.

Conclusions: The alteration of tumor microenvironment, such as cytoskeletal change and matrix remodeling via RhoA-YAP in CAFs, modulates OSCC progression. These understandings will provide the novel approaches for CAFs-based OSCC therapy.

OPG AND BCL-2 PROMOTE AMELOBLASTOMA CELL TUMORIGENESIS AND PREDICT PROGNOSIS FOR AMELOBLASTOMA PATIENTS.

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Ameloblastoma is the most frequent odontogenic epithelial tumor in the jaw. Though ameloblastoma belongs to benign odontogenic tumors, it exhibits a locally aggressive behavior with high recurrence rate. However, molecular markers predicting the recurrence have not been reported yet. The aim of this study was to find the prognostic markers in ameloblastoma. To detect apoptosis-related genes showing difference of expression level between ameloblastomas and normal oral tissues, the public database was analyzed. As results, OPG and Bcl-2 were identified as 2 most upregulated genes in ameloblastomas. To confirm public database analysis, in vitro study was conducted by use of AM-1 cell line. AM-1 cells expressed higher level of OPG and Bcl-2, compared with normal human epidermal keratinocytes (HEK). Exposing AM-1 cells to various environmental factors during culture in the 3-dimensional collagen gels were increased level of OPG and Bcl-2 than monoculture. To evaluate tumor-forming properties of AM-1 cells, subrenal capsule assay was conducted using AM-1 cells with hTERT-hNOF. As results, tumor formation were observed in 3 weeks, in which OPG and Bcl-2 expression was identified. To evaluate whether OPG and Bcl-2 regulates cell viability and apoptosis in AM-1 cells, siRNA transfection was conducted. As results, the knockdown of OPG and Bcl-2 reduced the cell viability and promoted the apoptosis of AM-1 cells. Knockdown of OPG and Bcl-2 decreased tumorigenesis. Eighty-nine cases of ameloblastomas were used for this study. Recurrence rate was 20.2%. Then, to validate whether these genes are associated to recurrence in ameloblastomas, immuno-histochemistry were performed. Each positivity classified 2 group by appropriate scoring system, low and high expression. The OPG and Bcl-2 expression was significantly associated with recurrence in conservative treatment group. These studies indicate that OPG and Bcl-2 status were independent predictive factors for recurrence.

10 YEAR REVIEW OF CHRONIC GRANULOMATOUS INFLAMMATORY REACTIONS FOUND IN THE ORAL CAVITY: 2007-2016.

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Chronic granulomatous inflammatory reactions are uncommon in the oral cavity. These lesions are reactive in origin and are characterized by macrophages which fuse to form multinucleated giant cells or transform into epithelioid histiocytes. Multiple etiologies exist for CGIR and include foreign body reactions to endogenous and exogenous materials, allergic

reactions, infectious diseases (fungal or bacterial), sarcoidosis, and Crohn's disease. Here we review CGIR seen over ten years and attempt to clarify their etiologies with the hope that this data will yield information which will allow us to better guide clinicians in the evaluation and treatment of their patients. A review of all cases of CGIR from New York Presbyterian/Queens between 2007-2016 was performed. After eliminating all lesions where foreign material or fungal organisms could be seen, 120 cases of CGIR were identified. Additionally, cases seen in conjunction with a lichenoid inflammatory infiltrate were excluded from the review as they warrant further, separate study. Using relevant clinical information submitted as well as responses to a ten-question survey sent to doctors which included questions regarding the etiology of the CGIR, medical work up, the presence of additional lesions, treatment, progression and recurrence, we identified the following information. Of the 120 cases, 56 were male and 64 were female. The age range was 3−88 years old. 122 sites were identified as some cases had multiple lesions. Only 13 of the 122 lesions were central in bone. The most striking findings was that 9 cases occurred under the age of 18 and all these were in males. Two of these patients had intrabony lesions. In this group, Crohn's disease was found to be the commonest etiology, seen in 5 patients. Therefore, the finding of granulomas, especially intrabony, in a young male warrants a gastrointestinal work up prior to an extensive medical evaluation.

IN VITRO EVALUATION OF THE ANTINEOPLASTIC EFFECT OF METFORMIN ON ORAL SQUAMOUS CELL CARCINOMA.

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Metformin is one of the most commonly prescribed drugs worldwide for the management of diabetes. Oral Squamous cell carcinoma is a public health problem worldwide and very little has been achieved regarding survival rates since the 1980s, despite some advancement in traditional treatment options. Metformin has demonstrated a citotoxic effect on neoplastic cells by inhibiting anabolism and stimulating catabolism. AMPK lead to inhibition of the mTOR pathway, thus reducing global protein translation and, therefore, slowing tumor progression.

Objectives: To evaluate the effect of metformin on viability and proliferation of oral squamous cell carcinoma cells in vitro.

Methods: Three cell lines were used, namely CAL27, HaCat and SCC4 (ATCC). The cutures were treated with a single dose of metformin at 10 mM and 20 mM. Cell proliferation and viability were evaluated at 24h and 48h using flow cytometry. Annexin V-FITC and propidium iodide (PI) were used to establish the rate of apoptosis and cell death, respectively.

Results: metformin proved cytotoxic with increased rates of apoptosis and cell death and in the HaCat (24.5% and 43%, respectively) and SCC4 lines (55% and 35%), especially at 20mM and 48h of treatment, except for the CAL27 line, which did not respond to the treatments.

Conclusion: Metformin caused cell death via apoptosis in oral squamous cell carcinoma cultures in vitro in a dose and time dependent manner.

PERICORONAL LESIONS OF UNERUPTED TEETH: EXPERIENCE IN 25 YEARS.

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Objectives: The aim of this study was to determine the epidemiology and clinical concordance of pericoronal lesions of unerupted teeth in biopsies of the Oral Pathology Laboratory of Universidad Peruana Cayetano Heredia (1991-2015).
A retrospective study was performed. Request forms for anatomical-pathological examination and histopathological slides were assessed. Data registered included: Age, sex, dental piece, presumptive and definite diagnosis. The WHO Classification (2017) was used for cysts and odontogenic tumors

Findings: 270 pericoronal lesions were found (1.69% of the total). There was relationship between the diagnoses and association to teeth (p=0.021), but not with position of the teeth and sex. It was present more in second and third decade of life (range: 5-80 years). The main histopathological diagnoses were dentiger cyst (40%) and normal dental follicle (23.7%). About pericoronal lesions, they mainly were located in inferior third molars (35.93%) and superior canines (21.85%). The concordance between presumptive and definitive diagnosis is low (Kappa=0.2536).

Conclusion: No concordance was found between presumptive and definitive diagnosis, it is the reason why the histopathological study in pericoronal lesions is very important.

A NEW HIGH-RESOLUTION INVASION TEST (HIT) CAN PREDICT MALIGNANT TRANSFORMATION IN ORAL EPITHELIAL DYSPLASIAS.

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Rationale: Detecting the earliest signs of invasion and predicting transformation in oral potentially malignant lesions (OPMLs) can facilitate earlier treatment of oral squamous cell carcinoma (OSCC) and decrease morbidity and mortality. Here we described a new test to diagnose early invasion and predict malignant transformation in OPML.

Methods: Fluorescent immunohistochemist and multichannel colocalization were used to identify invadopodia markers FISH, cortactin and MMP14 in OSCC and OPML. The presence of invadopodia markers was calculated using 3-channel colocalization analysis based on a custom algorithm developed using Volocity Software. The threshold for colocalization was determined by linear least-square fit of the channel intensities and the product of the difference of the means was (PDM) was used to compare the area of colocalization (HIT score). This algorithm was applied to 80 cases (10 cases of non-dysplastic hyperkeratosis, 22 cases of epithelial dysplasias (ED), 20 cases of OSCC and 28 cases from patients who progressed from ED to OSCC) to determine the overall validity of the approach and establish cut off values.

Results: There was a significant and progressive increase in the colocalization of invadopodia markers (HIT score) in dysplasias and OSCC compared to control. The results