medical history was significant for osteoporosis, but there was no history of anti-resorptive drug use. Upon examination, a gingival alveolar swelling was noted. Biopsy revealed high-grade adenocarcinoma, with immunohistochemical features most consistent with a breast primary. Subsequently, it was learned that the patient had a history of breast cancer, treated by total mastectomy of the left breast over three years previously with no previous evidence of metastases. The rarity of metastatic lesions to the jaw makes diagnosis particularly challenging. This case emphasizes the importance of assembling a thorough medical history as part of a complete patient work-up, especially in the presence of atypical symptoms or radiographic findings

THE TRANSITION OF TISSUE INHIBITOR OF METALLOPROTEINASE-4 TO -1 EXPRESSION MODULATES YAP/TAZ MEDIATED AGGRESSIVE PHENOTYPE IN LIPOSARCOMA. *DR. MADHU SHRESTHA, DR. TOSHINORI ANDO, DR. CHEA CHANBORA, DR. IKUKO OGAWA, DR. MUTSUMI MIYAUCHI, PROF. TAKASHI TAKATA. HIROSHIMA UNIVERSITY*

Objectives: Liposarcoma(LS) is the most common soft-tissue sarcoma. The histological spectrum has a well-differentiated-liposarcoma(WDLS) and a more aggressive dedifferentiated-liposarcoma(DDLS). Advanced therapeutic strategies based on molecular mechanism are urgently needed, especially for DDLS. Previously, we reported that TIMP-1 (a member of tissue-inhibitor-of-metalloproteinase), with its receptor CD63 activates yes-associated protein (YAP) and transcriptional co-activator with PDZ binding motif (TAZ) to promote cancer cell proliferation. Aberrant YAP/TAZ activation in LS is reported, however, contribution of TIMP-1-YAP/TAZ axis in LS remains unclear. Intriguingly, TIMP-4 is known to share CD63 as TIMP-1, but its role in LS is unknown. Here we clarified the expression and function of TIMP-1 and -4 through YAP/TAZ regulation in LS.

Materials & Methods: Cell lines of WDLS(94T778) and DDLS(SW872) were used for in vitro experiments such as Western blotting, RT-PCR, cell-proliferation, migration and apoptosis assay.

Results: Database analysis showed high TIMP-1 expression in DDLS patients correlating with poor prognosis, while high TIMP-4 expression in WDLS patients with better prognosis. TIMP-1 knockdown in DDLS cells inactivated YAP/TAZ and suppressed cell-growth, migration, which was rescued by constitutively active form of YAP5SA. On the other hand, cell-growth and migration were significantly increased in TIMP-1 over expressing WDLS cells, which was suppressed by verteporfin (a YAP/TAZ inhibitor). TIMP-4 knockdown in WDLS activated YAP/TAZ, promoted cell-proliferation and migration, which was inhibited by verteporfin treatment or YAP/TAZ knockdown. Recombinant TIMP-4 showed opposite results in DDLS cells significantly.TIMP-4 CD63 binding inactivated YAP/TAZ in WDLS.

Conclusion: The switching of TIMP-4 to -1 expression during transition from a WDLS to a DDLS led to activation of YAP/TAZ and promoted cell-proliferation, migration, inducing poor prognosis.

TIMP-1 and -4 as novel YAP/TAZ regulators may warrant future possibilities of targeting key molecules in development of diagnostic and therapeutic novelties in treating LS.

ARECA NUT EXTRACT ENHANCED M2-LIKE MACROPHAGE POLARIZATION AND FIBROBLAST ACTIVATION. *DR. LIEN-YU CHANG[A], MR. PO-JU HSIAO[B], MS. CHIH-YUN LU[B], DR. YI-CHUN LIN[C], PROF. SHAN-LING HUNG[B], PROF. YU-LIN LAI[C]. [A] NATIONAL YANG-MING UNIVERSITY, INSTITUTE OF ORAL BIOLOGY, DEPARTMENT OF DENTISTRY; TAIPEI VETERANS GENEAL HOSPITAL, DEPARTMENT OF STOMATOLOGY, [B] NATIONAL YANG-MING UNIVERSITY, INSTITUTE OF ORAL BIOLOGY, [C] TAIPEI VETERANS GENEAL HOSPITAL, DEPARTMENT OF STOMATOLOGY; NATIONAL YANG-MING UNIVERSITY, DEPARTMENT OF DENTISTRY*

Objectives: Areca nut chewing habit is popular in Taiwan and is closely related to oral squamous cell carcinoma (OSCC). Both activated fibroblasts expressing alpha-smooth muscle actin (α-SMA) and tumor-associated macrophages showing M2 polarization in stroma are supposed to be crucial in tumor progression. The purpose of the study was to examine the profile of stromal fibroblasts and macrophages in areca-associated oral cancer tissues, thein viro effects of areca nut extract (ANE) and two common oral insults, nicotine (NT) and lipopolysaccharides (LPS), on primary oral fibroblasts and human macrophages were also investigated. The study was approved by institutional Review Board of Taipei Veterans General Hospital, Taipei, Taiwan. Oral tissues were obtained with informed consent from patients undergoing routine surgical treatment.

Findings: Tissue sections showed that compared to the tumor-adjacent normal tissues (ANT), OSCC revealed a higher expression of pan-macrophage marker CD68, M2 markers CD163 and arginase-1 and activated fibroblast marker α-SMA, but not M1 marker CD86. In in vitro cell experiments, all of ANE, NT and/or LPS treatments could increase α-SMA expression and collagen production by oral fibroblasts. But only ANE treatment group, not NT or LPS group, enhanced the expression of M2 marker arginase-1 by macrophages. Furthermore, conditioned media acquired from macrophages (CM-Mac) of ANE treatment group increased the collagen production and IL-6 secretion by fibroblasts. CM-Mac of LPS treatment group also increased IL-6 secretion. Taken together, fibroblasts could be activated by ANE, NT and LPS, but only ANE could enhance macrophage M2-like polarization which in turn further increased fibroblast protein production.

Conclusions: Areca nut might compromise oral health by the setup of tumor-promoting microenvironment with local immune dysregulation via the enrichment of activated fibroblasts and M2-like macrophages.

INCREASED SOX2-POSITIVE CELLS IN BRAF (V600E) MUTATED AMELOBLASTOMAS. *DR. JULIA YU FONG CHANG[A], DR. CHIH-HUANG TSENG[B], DR. PEI HSUAN LU[A], DR. YI-PING WANG[A]. [A] NATIONAL TAIWAN UNIVERSITY HOSPITAL, [B] KAOHSIUNG MEDICAL UNIVERSITY HOSPITAL*

Objective: SRY related HMG box gene 2 (SOX2) is a transcription factor expressed in embryonic and adult stem cells. SOX2 positive dental epithelial stem cells have been shown to give rise to all dental epithelial cell lineages. Increased SOX2 expressing cells has been reported in ameloblastic carcinomas than ameloblastomas, which might indicate SOX2 contributes to the pathogenesis of ameloblastic neoplasms. Recent and our

previous studies have shown high frequency of BRAF(V600E) mutation in ameloblastomas. Interestingly, recent studies have reported that BRAF mutation is associated with the expression of SOX2 in colorectal cancers. Here, we investigated if SOX2-positive cell component is expanded in BRAF(V600E) mutated than wild type ameloblastomas.

Methods: Fifty-five formalin fixed paraffin embedded ameloblastoma tissue sections were used for macro-dissection of tumor component, DNA extraction and SOX2 immunohistochemistry. Sanger sequencing was further performed to detect the BRAF (V600E) mutation. The correlation between SOX2 positive cell numbers and BRAF status in ameloblastomas was evaluated by T-test.

Results: Among 55 ameloblastoma cases, forty-eight cases harbored BRAF(V600E) mutation. SOX2 positive cells were found in all cases regardless of BRAF status with average 22.3% SOX2 positive cells in ameloblastomas. BRAF(V600E) mutated ameloblastoma cases showed significantly more Sox2-positive cells (24.5%) than in wild type (6.6%) ($p<0.05$).

Conclusion: SOX2 positive cells were found in all ameloblastomas and BRAF(V600E) mutated ameloblastomas showed significantly more SOX2-positive cells. The results suggested BRAF(V600E) mutation may contribute to the expansion of SOX2 positive cell compartment.

CHONDROMYXOID FIBROMA OF THE MAXILLA: CASE REPORT.

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Objectives: Chondromyxoid fibroma (CMF) is a rare benign cartilaginous bone tumor with a characteristic lobular architecture and chondromyxoid background, this tumor account for 5% of all maxillofacial bone tumors.

Clinical presentation: we present a CMF of the left maxilla in a 15 years old female, presented with a bone swelling in the molar area, No systemic disease, other than hypothyroidism, were know. Tomographic evaluation exhibit a bone formatting lesion on the left maxilla, incisional biopsy was performed and processed histologically.

Histopathological diagnosis: Fibro-osseous lesion not otherwise specified.

Intervention: the patient was subjected to a left max-illectomy. A final diagnosis of CMF was emitted.

Outcome: the patient is treated by a Maxillofacial Prosthetics and close clinical follow up by the Oral and Maxillofacial Surgeon, the patient is 6 months free of disease.

Conclusions: Lesion was identified as Fibro-osseous lesion not otherwise specified by the incisional biopsy; it exhibited lobular architecture and chondromyxoid background, after the tumor resection the histopathological features were confirmed in the entire tumor, this case in particular exhibit extensive chondroid areas give the possibility of another diagnosis like: chondrosarcoma, chondroid osteosarcoma, chondroblastoma or chondroma.

BENIGN ALVEOLAR RIDGE KERATOSIS: CLINICOPATHOLOGICAL STUDY OF 174 CASES AND P53 EXPRESSION PATTERN.

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Objectives: Benign alveolar ridge keratosis (BARK) is a benign hyperkeratosis that occurs as a poorly demarcated white papule or plaque on the retromolar area or edentulous alveolar ridge mucosa caused by trauma. Histopathologic features are identical to cutaneous lichen simplex chronicus, a condition that results from chronic habitual skin scratching/picking. P53 protein is a tumor suppressor protein that plays a critical role in DNA repair. P53 protein has been shown to be present within 5-25% of the basal cell nuclei in normal oral mucosa and reactive lesions. The objective of this study is to report on the histopathologic features of BARK and to explore P53 expression pattern.

Study Design: Cases of BARK were identified from the biopsy service of the Harvard School of Dental Medicine from January, 2016 to December, 2017. Randomly selected cases were studied for the presence of P53.

Results: There were 174 cases comprising 119 males and 55 females (2.2:1; M:F) with a median age of 57 years (range 15-86). The majority were in the sixth (31.0%) and seventh (29.3%) decades. There were 112 (64.4%) cases on the retromolar pad and 62 (35.6%) on the edentulous alveolar mucosa; 27 (15.5%) cases were bilateral. Histopatho-logically, the oral mucosa showed hyperkeratosis often with wedge-shaped hypergranulosis and occasional focal parakeratosis. The epithelium exhibited mild to moderate acanthosis and slight surface undulations or papillomatosis, with tapered rete ridges, often confluent at the tips. The study for P53 performed in 11 cases showed less than 25 % nuclear positivity.

Conclusion: BARK is a distinct benign clinicopathologic entity caused by friction that is the intraoral counterpart of cutaneous lichen simplex chronicus with which it shares similar histopathologic features. It is not a mere hyperkeratosis which would relegate it to the clinical entity of leukoplakia, and which is a potentially malignant condition.

UNUSUAL DENTAL FOLLICULAR HAMARTOMA ASSOCIATED WITH A DENTIGEROUS CYST WITH FOCAL PARAKERATOSIS: A CASE REPORT AND REVIEW OF THE LITERATURE.

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Introduction: Dental follicular hamartoma with central odontogenic fibroma-like features is a rare condition that has been reported primarily in black African teenagers and young adults and is characterized by involvement of multiple teeth that either show amelogenesis imperfecta or enamel dysplasia, hypodontia, open-bite malocclusion, and gingival overgrowth.

Case Report: We report a case of an unusual dental follicular hamartoma associated with a dentigerous cyst in the left mandible of a 23-year-old male who was otherwise healthy. The patient presented to his oral surgeon with pain in the left mandible. Clinical examination revealed soft tissue swelling and suppuration associated with the distal aspect of tooth #18. A panoramic radiograph revealed a 3.3 cm x 2.3 cm unilocular radiolucency associated with impacted tooth #17 that extended from the superior aspect of the crown to the mandibular notch. This lesion had been present at least four years prior when it measured 2.6 cm x 2.0 cm. Tooth #17 was extracted and the bulk of the lesion was curetted. The biopsy revealed a cellular proliferation of spindled fibroblast-like cells in a