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.

DR. DO KYEONG KIM, DR. EUN KYOUNG KIM, PROF. JIN KIM. ORAL CANCER RESEARCH INSTITUTE, DEPARTMENT OF ORAL PATHOLOGY, BK21 PLUS PROJECT, YONSEI UNIVERSITY COLLEGE OF DENTISTRY, SEOUL, KOREA

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.

MS. JUEYOUNG KIM[A], MS. JINSUN KIM[B], DR. SHADAVLONJID BAZARSAD[C], PROF. SUNG-WON CHO[B], PROF. JIN KIM[C]. [A] ORAL CANCER RESEARCH INSTITUTE, DEPARTMENT OF ORAL PATHOLOGY, BK21 PLUS PROJECT, YONSEI UNIVERSITY COLLEGE OF DENTISTRY, SEOUL, KOREA, [B] DIVISION OF ANATOMY AND DEVELOPMENTAL BIOLOGY, DEPARTMENT OF ORAL BIOLOGY, YONSEI UNIVERSITY COLLEGE OF DENTISTRY, SEOUL, KOREA, [C] ORAL CANCER RESEARCH INSTITUTE, DEPARTMENT OF ORAL PATHOLOGY, YONSEI UNIVERSITY COLLEGE OF DENTISTRY, SEOUL, KOREA

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.

DR. RONALD FARAM, DR. PAUL FREEDMAN, DR. RENEE REICH. NEW YORK PRESBYTERIAN QUEENS

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