SAMADARANI SIRIWARDENA[B], PROF. RUWAN JAYASINGHE[B], PROF. JIN KIM[C], PROF. WANNINAYAKE TILAKARATNE[B]. [A] DEPARTMENT OF MEDICAL LABORATORY SCIENCE, FACULTY OF ALLIED HEALTH SCIENCES, UNIVERSITY OF PERADENIYA, SRI LANKA, [B] CENTER FOR RESEARCH IN ORAL CANCER, DEPARTMENT OF ORAL PATHOLOGY, FACULTY OF DENTAL SCIENCES, UNIVERSITY OF PERADENIYA, SRI LANKA, [C] ORAL CANCER RESEARCH INSTITUTE, DEPARTMENT OF ORAL PATHOLOGY, YONSEI UNIVERSITY COLLEGE OF DENTISTRY, SEOUL, KOREA

Objectives: Areca-Nut (AN) induced Oral Premalignant Diseases (OPMDs) are a health burden in Asian countries which causes higher morbidity and mortality. Oral Submucous Fibrosis (OSMF) and Oral Leukoplakia (OL) are the most vulnerable AN induced OPMDs which have a considerable malignant transformation rate. The underline mechanism of the carcinogenesis in OPMDs is still obscure. It was found that the oxidative stress caused by the AN can induce the carcinogenesis in OPMDs. Based on our previous research, it was found that some of these OPMDs have DNA damage caused by oxidative stress. Tropical countries are rich of herbs with antioxidants. Our attempt was to test few herbs as a remedy to reverse the potential carcinogenesis in AN induced OPMDs by reducing the oxidative stress caused by the AN.

Findings: Expression of Phospho histone H2AX, DNA double-strand breaks (DNA DSBs) marker was tested immunohistochemically in OPMDs with the history of AN consumption and compared with normal oral mucosa (NOM) and oral squamous cell carcinoma (OSCC). Phospho histone H2AX was significantly increased in OL and OSMF compared to the NOM ($p<0.05$). In-vitro studies using immortalized human oral keratinocytes (IHOK) shown that AN induced reactive oxygen species (ROS) production can be significantly reduced by the ethanol extracts of the antioxidant rich herbs Shumacheria castaneifolia leaves (SC-extract) and Solanum nigrum linn leaves (SN-extract). Antioxidant properties of the herbs were analyzed by DPPH assay. Furthermore, the amount of Phospho histone H2AX in response to 24hr AN treatment was considerably reduced in pretreated IHOK cell with SC extract. Murine model experiment also revealed that the herbal extracts can reduce the AN induced DNA DSBs in oral mucosa.

Conclusions: This study is evident that blocking ROS generation by herbal extracts as a promising approach to reverse DNA DSBs caused by AN. Especially, to prevent malignant transformation in OPMDs

MICRORNA-222 AND MICRORNA-203 SIGNATURES IN ORAL SQUAMOUS CELL CARCINOMA: POTENTIAL ROLE IN PROGRESSION AND AS THERAPEUTIC TARGETS.

DR. MADHURA MG. DAPM R V DENTAL COLLEGE AND HOSPITAL, BENGALURU, KARNATAKA, INDIA

Objectives: To discuss the proposed role of microRNA-222 (miR-222) and microRNA-203 (miR-203) in oral squamous cell carcinoma in the progression and as possible therapeutic targets.

Findings: miR-222 is colocalized as a cluster in the short arm of chromosome X. Luciferase reporter gene assays in oral tongue squamous cell carcinoma (OTSCC) have shown that hsa-miR-222 regulates the MMP1 expression through both direct cis-regulatory mechanism (targeting MMP1 mRNA) and indirect trans-regulatory mechanism (indirect controlling of MMP1 gene expression by targeting SOD2). Hence, hsa-miR-222 might serve as a novel therapeutic target for OTSCC patients at risk of metastatic disease.
miR-222 has been shown to regulate TRAIL resistance and enhancement of tumorigenicity through PTEN and TIMP3(Tissue inhibitor of metalloproteinase 3) downregulation.
miR-222 has been implicated to target PUMA(p53 up-regulated modulator of apoptosis) to improve sensitization of UM1 cells to Cisplatin.
miR-203 acts as a molecular switch between keratinocyte proliferation and differentiation in adult epidermis by targeting ΔNp63 mRNA. Following DNA damage, ΔNp63 downregulates and a possible activation of the apoptotic program in head and neck squamous cell carcinoma has been thought of.
miR-203 has been shown to target EIF5A2 in colorectal cancer cells. Serving as a tumor suppressor gene, miR-203 has been thought to be a useful potential therapeutic target in colorectal cancer. miR-203 as a therapeutic target in oral squamous cell carcinoma needs further validation.

Conclusion: In tumour progression, several cellular pathways may be affected by a single microRNA since it can target multiple mRNAs. Much more light is to be shed by developing as well as by tracking the identified microRNA signatures in oral squamous cell carcinoma, to pave the way for their future clinical use in the diagnosis, management, and prognosis.

LADININ-1 IS INVOLVED IN CELL MOTILITY AND PROLIFERATION OF ORAL SQUAMOUS CELL CARCINOMA CELLS.

DR. TATSUYA ABE[A], DR. MANABU YAMAZAKI[B], DR. SATOSHI MARUYAMA[C], PROF. YOICHI AJIOKA[A]. [A] DIVISION OF MOLECULAR AND DIAGNOSTIC PATHOLOGY, NIIGATA UNIVERSITY GRADUATE SCHOOL OF MEDICAL AND DENTAL SCIENCES, [B] DIVISIONS OF ORAL PATHOLOGY, DEPARTMENT OF TISSUE REGENERATION AND RECONSTRUCTION, NIIGATA UNIVERSITY GRADUATE SCHOOL OF MEDICAL AND DENTAL SCIENCES, [C] ORAL PATHOLOGY SECTION, DEPARTMENT OF SURGICAL PATHOLOGY, NIIGATA UNIVERSITY HOSPITAL

Objectives: Oral squamous cell carcinomas (SCCs) and carcinoma in-situ frequently form the interface between cancer and non-cancerous epithelium. Previously, we identified the altered expression of 7 specific proteins around the interface between cancer and non-cancerous epithelium using proteome analysis of oral SCC tissue sections. Among identified proteins, ladinin-1 (LAD1) expression was significantly increased in the cancer tissue adjacent to non-cancerous epithelium. However, the function of LAD1 in oral SCCs is totally unknown. Thus, the aim of this study was to examine the function of LAD1 in the oral SCCs by in-vitro analysis.

Findings: The gene and protein expressions of LAD1 were confirmed by quantitative PCR and western blotting in three oral SCC cell lines, HSC-2, -3, and -4. Using immunofluorescence, LAD1 was localized in the peripheral area of the cytoplasm of cancer cells. High resolution morphological analysis using structured illumination microscopy revealed that LAD1 was co-localized with actin filament forming “actin arc” in the