

Expression of γ -h2ax and p53 in oral cancer and oral potentially malignant diseases with areca nut history

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DNA double strand breaks (DSBs) marker γ -H2AX and tumor suppressor p53 are direct substances and central players in cellular DNA damage responses (DDR). Emerging evidence suggests that an intact DDR serves as a potent barrier for malignant transformation. The aim of this study was to analyze γ -H2AX and p53 expressions in oral cancer and oral potentially malignant diseases (OPMDs) with Areca Nut (AN) history.

Immunohistochemically, we investigated DDR by analyzing expressions of γ -H2AX and p53 in OPMDs. We utilized 15 each archival biopsy samples of oral leukoplakia (OL), oral submucous fibrosis (OSMF) and oral squamous cell carcinoma (OSCC) with the history of AN consumption. We also observed AN induced DNA DSBs in cancer cell lines using fluorescence activated cell sorting (FACS) analysis. Statistical evaluation was done by Fisher exact test and p value <0.05 considered as significant.

γ -H2AX accumulated in OL ($p = 0.002$), OSMF ($p = 0.000$) and OSCC ($p = 0.000$) significantly compared to the normal oral mucosa (NOM). Among OPMDs, H2AX phosphorylation is significantly low in OL, but its level peaked in OSCCs ($p = 0.032$). Also p53 was significantly expressed in OL ($p = 0.000$), OSMF ($p = 0.000$) and OSCC ($p = 0.000$) compared to NOM. In contrast to the findings of γ -H2AX, both OL ($p = 0.013$) and OSMF ($P=0.028$) denoted lower expressions of p53 compared to OSCC. We also noted that there was a positive correlation between two biomarkers in our samples ($p = 0.000$). In-vitro studies showed γ -H2AX accumulation in YD38 ($P = 0.12$) and HSC2 ($p=0.028$) cancer cells increased following AN treatment.

Our results suggest that the expression of γ -H2AX and p53 is predominant in OSCCs compared to non-transformed oral mucosal tissues and in-vitro data provides strong evidence that AN is responsible for that evoked response. Furthermore, DNA damage occurs in early stages of oral pre-cancer and increased during the course of oral carcinogenesis. Thus, our findings suggest that combined expressions of γ -H2AX and p53 can be used as a tool for early detection of oral cancer in patients with the history of AN consumption.