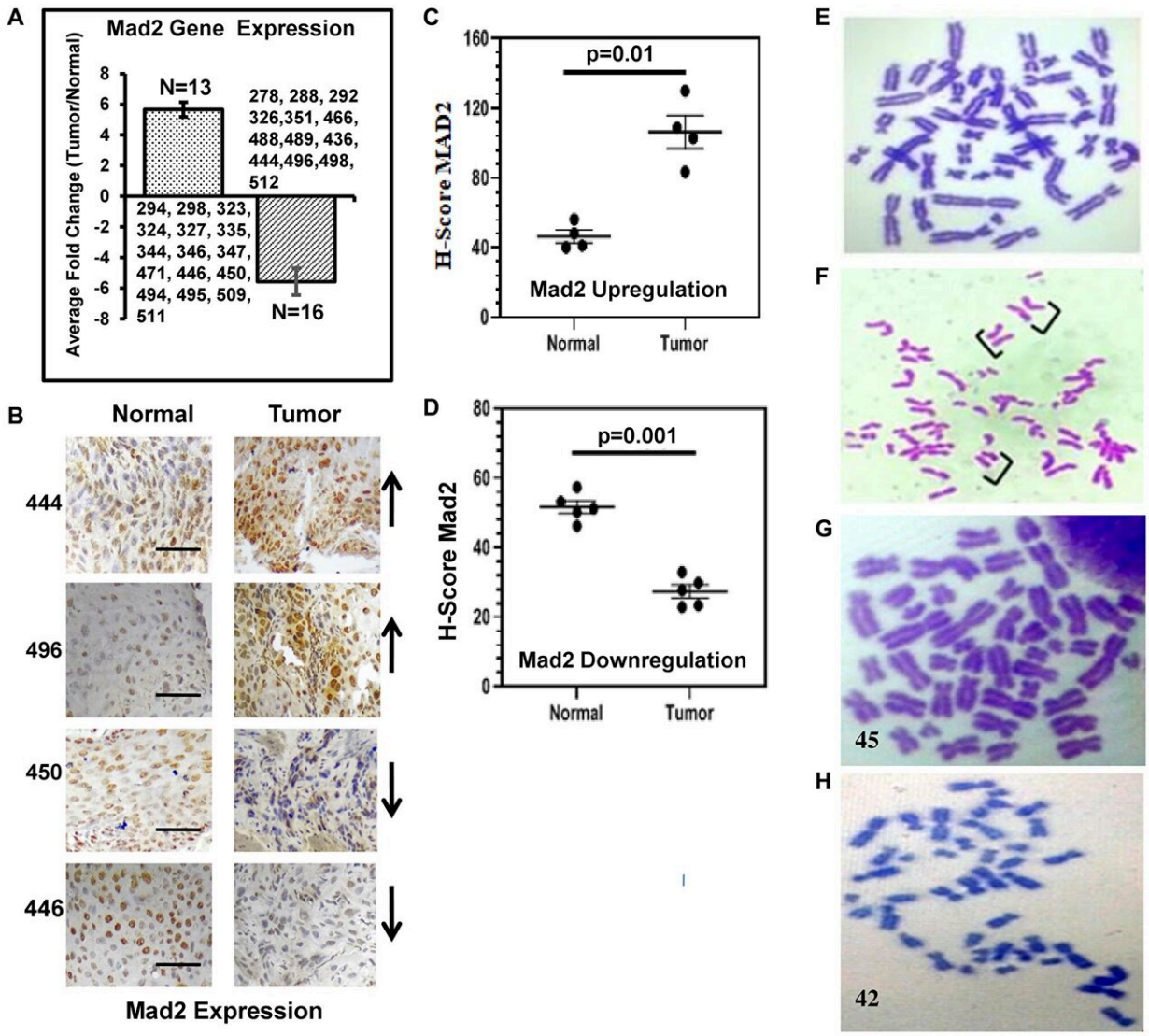
Differential expression of Mad2 gene in human esophageal cancer

February 12 2024



Expression analysis of the human Mad2 gene and karyotype analysis of genomic instability in esophageal cancer patients. (A) Expression of Mad2 gene in

esophageal cancer tissues analyzed by qRT-PCR. Patients ID numbers are shown. (B) Representative images of an immunohistochemical (IHC) analysis of tumor and adjacent normal tissues in ESCC done with anti-Mad2 antibody. Patients ID numbers are shown in the left side. Arrows indicate the upregulation and down regulation of Mad2 expression in the tumor tissues. The magnification of all these images is 40x. (C, D) Scatterplot of H-scores based on IHC for Mad2 positive cells in Mad2 upregulation and Mad2 downregulation groups, respectively. (E) Normal metaphase spread from human PBLs. Data were analyzed using one-way ANOVA with Tukey's multiple comparison post-tests. P values less than 0.05 are considered significant. The scale bar: 200 μm. (F) Premature sister-chromatid separation in PBL of esophageal cancer patients. Brackets show sister chromatids lying separated in mitotic figures that show the phenotype. (G, H) Metaphase spread showed 45 and 42 chromosomes in PBLs of esophageal cancer patients, respectively. Credit: *Oncotarget* (2024). DOI: 10.18632/oncotarget.28554

A new research paper titled "Differential expression of Mad2 gene is consequential to the patterns of histone H3 post-translational modifications in its promoter region in human esophageal cancer samples" has been published in *Oncotarget*.

Raw areca nut (AN) consumption increases esophageal squamous cell carcinoma (ESCC) due to overexpression of securin (pituitary tumor transforming gene1), causing chromosomal instability. Mitotic arrest deficient protein 2 (Mad2), a crucial spindle assembly checkpoint protein, is at risk of aneuploidy and tumor development when overexpressed or underexpressed.

In this new study, researchers Chongtham Sovachandra Singh, Nabamita Boruah, Atanu Banerjee, Sillarine Kurkalang, Pooja Swargiary, Hughbert Dakhar, and Anupam Chatterjee from The Assam Royal Global University, University of Pennsylvania, LN Mithila University,

University of Chicago Medicine, Nazareth Hospital, Laitumkhrah, and North-Eastern Hill University evaluated Mad2 status in human ESCC with AN consumption habits, revealing unclear molecular mechanisms.

Human ESCC samples (n = 99) were used for loss of heterozygosity analysis at 4q25-28, while 32 samples were used for expression analysis of Mad2, E2F1 genes, and Rb-phosphorylation. Blood samples were used for metaphase preparation. The Mad2 deregulation was assessed using chromatin immunoprecipitation-qPCR assay in the core promoter region, establishing its association with the pRb-E2F1 circuit for the first time.

"The study revealed overexpression and underexpression of Mad2, premature anaphase, and chromosome missegregation in all the samples," the researchers write.

LOH pattern identified a deletion in D4S2975 in 40% of ESCC samples. The study reveals the deregulation of pRb-E2F1 circuit in all samples. 4q27 disruption could be a factor for Mad2 underexpression in AN-induced esophageal carcinogenesis, while overexpression may be due to the deregulation of the Rb-E2F1 circuit and consequently elevation of H3K4me3 and H3K9ac.

"Mad2 expression levels with chromosomal abnormalities can be a clinical biomarker, but further research is needed to understand pRb's role in Mad2 down-regulation," the researchers conclude.

More information: Chongtham Sovachandra Singh et al, Differential expression of Mad2 gene is consequential to the patterns of histone H3 post-translational modifications in its promoter region in human esophageal cancer samples, *Oncotarget* (2024). DOI: 10.18632/oncotarget.28554

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