POSSIBLE ROLE OF CRY1 AND CRY2 IN ORAL CARCINOGENESIS

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Aim. Dysfunction of the circadian clock is involved in tumorigenesis, and altered expression of some clock genes has been found in cancer patients. It has been shown recently that the occurrence, development, prognosis, and treatment of cancer are closely related to the abnormal expression of certain circadian-clock genes. CRY1 and CRY2 circadian-clock gene plays an important role in the regulation of many normal physiological rhythms. This proteins act as light-independent inhibitors of CLOCK-BMAL1 components of the circadian clock. It has been revealed recently that abnormal expression of CRY1 and CRY2 correlate closely with the occurrence and development of many cancers. However, the expression and significance of this proteins in oral squamous cell carcinoma (OSCC) remains unknown. The aim of this study was to evaluate the expression levels of CRY1 and CRY2 in oral cancer.

Materials and methods. CRY1 and CRY2 expression in cancerous and peritumoral tissues (when it was present) from 27 patients with OSCC was detected by immunohistochemistry techniques. Of all samples were received medical records (age, sex, grading, TNM, site of localization of the tumor). Immunohistochemistry was then performed on two sections for each of 27 sample mounted on poly-L-lysine-coated glass slides to evaluate respectively the expression of CRY1 and CRY2.

Results. In this study, out of the 27 cases, 11 were +/- positive in tumor area for CRY1 (most of which are well differentiated), while out of 23 cases in which we evaluated the peritumoral tissue present in the section, 18 were positive. Also in the cases of positive tumor, almost always cytoplasmic, the CRY1 appears to be more strongly positive in dysplastic areas or even more in healthy epithelium, with a negative regulation in the areas most undifferentiated. As for the CRY2, out of the 27 cases analyzed, 17 were positive in the tumor area while about 23 cases in which we evaluated in peritumoral tissue present in the sections, 20 cases were positive. In tumor epithelium were found positivity also medium / high, present in tumors of different degree of differentiation, in some cases in other nuclear or cytoplasmic and nuclear/cytoplasmic, but when present the CRY2 is expressed, in most cases, in a manner similar or more intensely in peritumoral dysplastic epithelium. In the case of CRY2, there were no positivity in healthy epithelium (when present), but only in dysplastic epithelium. In addition, the positivity observed especially in peritumoral epithelium were present in states intermediate/surface.

Conclusions. In conclusion, abnormal expression levels of CRY1 and CRY2 in OSCC tissue compared to healthy or dysplastic tissue may be related to the process of tumorigenesis. Further research focusing on these genes may, from the perspective of biological rhythms, provide novel ideas and methods for a better understanding of the occurrence and development of tumors, and for treatment of oral cancer.