

*Extended Abstract*

# **TIMELESS in Head and Neck Squamous Cell Carcinoma: A Systematic Review <sup>†</sup>**

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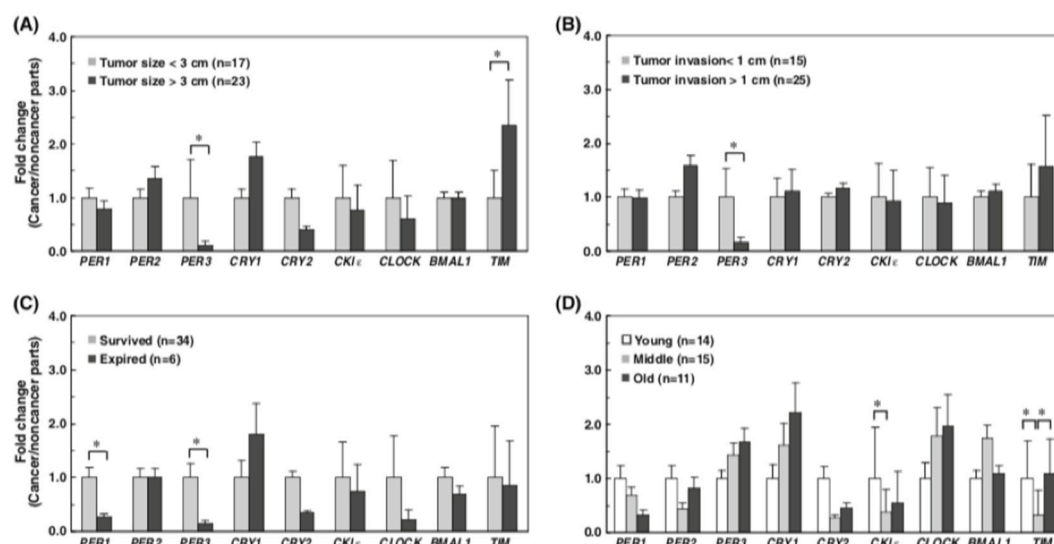
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TIMELESS is one of the main circadian genes. Different roles are described, such as replication fork stability, cell survival after DNA damage or replication stress by promoting DNA repair. TIMELESS deficiency increases genomic instability and its reduction increases Rad51 and Rad52 foci formation during S phase [1]. TIMELESS and PARP1 operate in a complex to mediate DNA repair. It is also showed that alteration in circadian rhythm is associated with cancer development and tumor progression, such as chronic myeloid leukemia, hepatocellular carcinoma, and breast cancer [2]. We wanted to summarize the role of TIMELESS in head and neck squamous cell carcinoma. To do so, we performed a literature review using these keywords: TIMELESS [All Fields] AND (“neoplasms” [MeSH Terms] OR “neoplasms” [All Fields] OR “cancer” [All Fields]). We found 54 studies. At the end of the selection process, 4 studies were considered suitable for the analysis of TIMELESS in HNSCC. In Ao et al. TIMELESS resulted downregulated in a HNSCC cell line. In Bjarnason’s study [3] through TS Enzyme Activity confirmed its downregulation in biopsy model. Hsu in 2011 [4] used real-time quantitative RTN-PCR on 40 tissue samples with HNSCC to clarify whether the expression levels of circadian clock genes were altered in tumor tissues. Data demonstrated that the expression levels of PER1, PER2, PER3, CRY2, and BMAL were significantly downregulated in HNSCC ( $p < 0.01$ ) (Figure 1), showing its dysregulation in cancer. TIMELESS seems to play an important role in cancer and further investigations are needed to investigate its role as prognostic marker or pharmaceutical target.



**Figure 1.** Tumor conditions and circadian clock gene expression in HNSCC patients. Tumor size (A), tumor invasion (B), survival (C) and age (D) of the 40 HNSCC patients were correlated to the expression of the nine circadian clock genes. The y axis represent the relative mRNA expression level. The relative expression in cancerous tissues is calculated by  $\Delta\Delta Ct$ . The expression in tumor size < 3 cm (A), tumor invasion < 1 cm (B) and survival (C) is designated 1, and the relative expression in tumor size > 3 cm (A), tumor invasion > 1 cm (B), and expire (C) is calibrated to obtain the folds changed, respectively Statistical significance \*  $p < 0.05$  evaluated with  $t$  test.

**Conflicts of Interest:** The authors declare no conflict of interest.

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