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"Will timing of Chemotherapeutic drug administration matters in the treatment of oral squamous cell carcinoma? – Unlocking the knowledge and the application of Chronotherapeutics"

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Oral squamous cell carcinoma (OSCC) ranks as the sixth most widespread cancer worldwide, characterized by elevated morbidity and mortality rates. Among individuals of all ages, India has the highest rate of head and neck oral squamous cell carcinoma (HNSCC) when it comes to culturally included tobacco and arecanut habits. In addition to well-established risk factors such as tobacco consumption, HPV infection, and various lifestyle factors, it is a must to acknowledge the contribution of disruptions in the circadian rhythm to the pathogenesis of OSCC (Rahman *et al.*, 2019).

Biological species have circadian clocks inorder to preserve homeostasis, which allow them to adjust and adapt accordingly to changes in their environment naturally. Disruptions in the circadian rhythm and the chronic diseases including cancer are intimately associated. The suprachiasmatic nucleus (SCN) of the hypothalamus and peripheral clocks make up circadian clocks. Numerous malignancies exhibit variable expression of circadian clock genes, which hasten the growth and spread of tumors. Also one should understand the fact that the different kinds of tumor cells express clock genes differently and differences exist in the circadian rhythms between normal and tumor tissues and between individuals (Poornachitra*et al.*, 2023).

Literature showed that Circadian locomotor Output cycles Kaput (CLOCK), Period (PER), Cryptochrome (CRY), Brain and Muscle aryl hydrocarbon receptor nuclear translocator 1 (BMAL1) were found as the key genes associated with the etiopathogenesis, invasion, local as well as distant metastatic spread of OSCC. The dimerization of CLOCK and BMAL1, which is the central component of the molecular circadian mechanism, consequently enhances transcription of multiple genes related to circadian rhythm including PER and CRY. Eventually, the formation of these complexes leads to the suppression of CLOCK and BMAL1 that in turn results in the establishment of a cellular feedback-maintaining circadian rhythm regulatory loop. The precise regulation of gene expression is the mechanism instrumental to the circadian clock exerting its vital influence on numerous physiological processes such as the cell cycle, metabolism, and DNA damage repair. These processes therefore play a central role in the maintenance of cellular homeostasis (Zhou *et al.*, 2021).

Any molecular disruptions in the Circadian genes function or of their expression was among the factors that lead to modified circadian cycle which may consequently result in uncontrolled cell proliferation, failure of apoptosis, and an increased neoplastic transformation of cells in OSCC. Among studies, the reported is that influence of CLOCK change directly on cell cycle regulation while setting of BMAL1 expression as decreased ability in DNA repair has been linked to genetic instability, one of the hallmarks of cancer cells (Kinouchi*et al.,* 2020).

Additionally, PER/CRY protein misguidance through which the role of PER and CRY proteins in tumor suppression can disrupt and could aid in the onset of cancer. Evidence has shown that such factors not only superimpose the onset of OSCC, but they also become part of advanced stages which include invasion, metastasis, and tumor spread. Through the modulation of these circadian genes expression or function, it holds potential not only for the prevention of OSCC but also for novel treatments aimed at reducing the aggressive behaviour of established tumors (Nirvani*et al.,* 2018).

Conventional treatments of OSCC like surgery, chemotherapy, and radiation therapy often lack specificity leading to significant side effects, resistance development, high toxicity to the adjacent healthy tissues and limited efficacy. Chronotherapeutics is the practice of administering treatments in a way that maximizes therapeutic benefit and minimizes side effects by taking into account the patient's individual circadian cycles. Body temperature, hormone secretion, autonomic nervous system activity, cytokine release, and resting-activity act as biomarkers of the Circadian Timing System (CTS) to optimize precise timing and dosing of chronotherapy in cancer patients. Monitoring these circadian rhythms helps identify the best timing for delivering anticancer treatments, enhancing efficacy and reducing side effects.

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REFERENCES:

Kinouchi, K. and Sassone-Corsi, P. (2020). Metabolic rivalry: circadian homeostasis and tumorigenesis. *Nat Rev Cancer.*, 20(11):645-661. https://doi.org/10.1038/s41568-020-0291-9.

Nirvani, M., Khuu, C., Utheim, T.P., Sand, L.P. and Sehic A. (2018). Circadian clock and oral cancer. *MolClinOncol.*, 8(2):219-226. https://doi.org/10.3892%2Fmco.2017.1518

Poornachitra, P., Muthukrishnan, A. and Devaraj, E. (2023). Chronotherapeutics in the management of oral squamous cell carcinoma - A futuristic novel treatment strategy. *Indian J Cancer.*, 60(4):595-596. https://doi.org/10.4103/ijc.ijc_19_23.

Rahman, S., KraljevićPavelić, S. and Markova-Car, E. (2019). Circadian (De)regulation in Head and Neck Squamous Cell Carcinoma.*Int J Mol Sci.*, 20(11):2662. https://doi.org/10.3390/ijms20112662.

Zhou, J., Wang, J., Zhang, X. and Tang, Q. (2021). New Insights into Cancer Chronotherapies. *Front Pharmacol*,12:741295. https://doi.org/10.3389/fphar.2021.741295