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Illuminating The Shadows: Unveiling The Concealed Hazards And Intriguing Links Between Light Pollution And Cancer

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Abstract

Shift workers who work at night have been shown to be more at risk for lung, breast, colorectal, and prostate cancers when exposed to artificial light at night (ALAN). Human cancer has been linked to light pollution's disruption of the circadian cycles. Light deprivation reduces carcinogenesis, but an impairment of pineal gland function caused by exposure to a steady light regimen enhanced carcinogenesis. Due to its capacity to stop the cyclic nightly generation of melatonin, artificial light exposure has been hypothesised to be a risk factor for breast cancer in these industrialised nations. Wonder chemical melatonin, sometimes known as the "hormone
of darkness," is thought to have a role in many physiological functions and anomalies, such as the regulation of sleep, circadian rhythms, retinal physiology, seasonal reproductive cycles, immune activity, antioxidation and cancer. Telomerase is impacted by light pollution in a number of ways, including indirectly through melatonin. The expression of Telomerase Reverse Transcriptase (TERT) mRNA is first inhibited by melatonin. Second, by blocking NFκB p50/p65 nucleus translocation and their binding to the promoters of human telomerase reverse transcriptase (hTERT) and inducible nitric oxide synthase (iNOS), melatonin increases the antitumor effect of a drug similar to vemurafenib. This suppresses the expression of iNOS and hTERT.

Keywords – Light Pollution, Cancer, Melatonin, hormone, telomerase, reverse transcriptase

Introduction:

For 3 to 4 billion years prior to the creation of electric lighting, life on Earth evolved under the defined pattern of light during the day and darkness at night. Over time, nearly all species, including humans, have absorbed the Earth's rotational rhythm, leading to the creation of self-sustaining biological clocks that synchronize physiology and behaviour to roughly match the duration of a solar day. Almost all biological functions, in fact, have functional cycles that are close to 24 hours long. Circadian rhythms are endogenous, self-sustaining rhythms of optimum function that are regulated to precisely 24 hours per day by exposure to light during the day (Bell-Pedersen et al., 2005; Drake & Wright, 2011; Shostak, 2017).

Mammalian circadian rhythms include the sleep-wake cycle, body temperature, and behavioural patterns. Notably, circadian rhythms regulate a number of critical cancer-related activities. For example, cell division has separate daily cycles. Circadian rhythms and cell division are inversely connected. The disturbance of circadian rhythms has a substantial influence on cancer growth and cell division, whereas malignant transformation disrupts circadian structure. Exposure to light at night, working night shifts, and the so-called "social jet lag" that happens when sleep and waking cycles are switched between weekends and workdays are all common modern disruptors of circadian rhythms. The molecular circadian clock mechanism, as well as the importance of daylight during the day and darkness at night, are discussed briefly here (Bell-Pedersen et al., 2005; Drake & Wright, 2011; Shostak, 2017).

In mammals, the master circadian clock is the hypothalamic suprachiasmatic nuclei (SCN), which is at the top of a hierarchy of independent endogenous time-keepers. The SCN has 20,000-50,000 closely packed small neurons in humans and rats and is located just above the optic chiasm. The SCN is a complex cell structure that includes a variety of peptides and neurotransmitters. Despite the fact that the SCN, as previously stated, serves as the master circadian clock at the top of a hierarchically structured system, circadian oscillators may be found in practically all tissues of multicellular organisms. Tissue-specific clocks, which resemble circadian oscillators in the SCN in molecular structure, include the molecular machinery necessary for self-sustaining cycles. The SCN synchronizes peripheral clocks with the outside world through neuronal, hormonal, non-SCN, and other signals. The circadian rhythms of clock genes, metabolism, immune response, hormone production, and reproductive function in rats are all disturbed by artificial light at night (ALAN). which in particular have a great deal to do with the division and growth of cells. This has led to a current focus in basic science research on the effects of artificial light on circadian rhythms and oncogenesis during the night (Lydic, Albers, Tepper, & Moore-Ede, 1982; Takahashi, 2004; Walker et al., 2020).

Cell Cycle and the Circadian Clock:

In regularly developing mammalian cells, the normal circadian clock and cell cycles are phase-locked. The molecular foundation of the coupling between these two cycles is shown by several comparable regulatory mechanisms, albeit much remains to be discovered about this relationship. First, it's important to understand how the cell cycle and the circadian cycle are influenced by each other. The circadian clock regulates the cell cycle in general by controlling the unidirectional progression through the stages of the cell cycle through the interaction of molecular circadian clock elements, cyclin-cyclin-dependent kinase (CDK) complexes, and cell cycle inhibitors at the transcriptional or protein level. Brain and muscle Arnt-like protein-1 (BMAL1)-CLOCK (circadian locomotor output cycles kaput) regulates the transcription of c-Myc, which regulates the start of the G1 phase of the cell cycle. Lastly, WEE1 regulates the circadian rhythm of the CLOCK-BMAL1-controlled Cyclin B-CDK1 complex. When considered together, the circadian clock controls transitions between every step of the cell cycle. DNA damage, which may be mediated by Cryptochrome, has the ability to reset the circadian clock (Gréchez-Cassiau, Rayet, Guillaumond, Teboul, & Delaunay, 2008; Kowalska et al., 2013; Papp et al., 2015).

In addition to reciprocal regulation across cyclic pathways, the circadian clock and cell cycle pathways share shared enzyme regulators in the phosphorylation and ubiquitination processes. It's possible that these post-transcriptional changes function as coupling and common regulatory mechanisms. The ubiquitination of F-box protein FBXW7 leads to the degradation of CRY2 in the circadian clock, REV-ERB in the cell cycle, and Cyclin E in these processes. WEE1 in the cell cycle and PER1 and 2 in the clock can be destroyed by phosphorylation via CK1, although PER2 and WEE1 can also be degraded by E3 ubiquitin ligase -TRCP. When GSK3 is phosphorylated, BMAL1 and cyclin D1 are both broken down, whereas REV-ERB remains stable. Furthermore, the cell cycle protein p27 is stabilized by AMPK-mediated phosphorylation, but the circadian clock protein CRY1 is destabilized. Post-transcriptional modifiers can have both complimentary and opposing effects on circadian clock and cell cycle rhythms, which can control each other reciprocally. Dysregulation in the common regulatory and coupling links between the two pathways, either separately or in combination, can lead to tumorigenesis (Fang et al., 2015; Walker et al., 2020; Zhao et al., 2016).

Disrupted Circadian Rhythms and Cancer:

The scientific community has conjectured that disruptions to circadian rhythms might raise the risk of cancer since the late 20th century. Among other modern circadian rhythm disruptors, ALAN exposure's effects on carcinogenesis have drawn special interest because of its growing worldwide significance. Because of its disruptive effects on endocrine function, ALAN exposure has drawn a lot of attention to the relationship

between breast and prostate cancers. Because there are clear ethical issues with causal ALAN and cancer investigations, the majority of our information regarding ALAN exposure as a risk factor for cancer in people comes from epidemiological observational, case-control, and cohort research study. At the time, in vitro and animal studies demonstrated the beneficial benefits of melatonin supplementation on tumor development. This gave rise to several ideas, one of which was that exposure to ALAN suppresses melatonin rhythms, thereby increasing the prevalence of breast cancer (Fonken, Aubrecht, Meléndez-Fernández, Weil, & Nelson, 2013; Mhatre, Shah, & Juneja, 1984; van den Heiligenberg et al., 1999).

Numerous sorts of circadian rhythm disturbances, including poor meal timing, social jet lag, lack of sleep, and exposure to ALAN, are common among shift workers. This makes it difficult to discern between the disrupting aspects of shift work and those that have negative physiological effects, including an increase in the prevalence of cancer. Consequently, we have to be cautious when interpreting the results because most shift-work epidemiological studies do not directly examine the effects of ALAN on physiology. On the other hand, the results of these human studies can provide an objective viewpoint about the potential impact of shift work-induced circadian rhythm disturbance and its behavioral consequences, such as exposure to ALAN, on cancer risk. Studies on the relationship between shift work and breast cancer indicate that the longer a person works shifts, the higher their risk becomes. A pioneering study on shift employment examined the incidence of breast cancer in Norwegian women over 50 who worked as telegraph operators. A greater odds ratio was seen after taking employment length into account, although it lost statistical significance. According to an additional study, women who worked more than half of the year principally (>60%) night shifts had a significantly increased risk of breast cancer. An increased risk of breast cancer was shown to be associated with any experience of graveyard shifts, and the risk increased with the number of years of shift work, according to a case-control study of female shift workers in the US across a range of jobs. The same study suggests that sleep deprivation may marginally increase your chance of breast cancer development. Shift employment was shown to increase the risk of breast cancer in women who worked rotational night shifts for more than 20 years in the case of premenopausal women and more than 30 years in the case of postmenopausal women. A third case-control study of female nurses in Norway, like the previous one, did not find any statistically significant increase in breast cancer risk among women who had worked shifts for more than thirty years. To obtain a little more filtered view of how ALAN influences cancer incidence, other researchers have examined cancer incidence rates in individuals who are blind. Exposure to ALAN should not disrupt melatonin and other circadian rhythms in individuals without functional retinal circuitry that transmits light signals to the SCN and other components of the circadian system. Although this explicit hypothesis (i.e., blind shift workers and cancer incidence, or link between blindness, ALAN exposure, and cancer) has not yet been explicitly evaluated, some study has examined the incidence of cancer in the blind population. Two international studies on ALAN and breast cancer incidence have been conducted. Using the GLOBOCAN 2002 database, Kloog et al. found a substantial connection between ambient ALAN levels and breast cancer. In 2015, a different group conducted follow-up research and discovered that the original relationship between ALAN and the risk of breast cancer was moderate and not statistically significant. However, when nations were categorized into Western, Gulf State and Southeast Asian, and "Other," the relationship between ALAN and breast cancer incidence was statistically significant once again. Using satellite ALAN data, the same researchers found a connection between men's increased prostate cancer risk and ALAN, but not for lung or colon cancer. Observational research employing satellite ALAN data indicated a significant correlation between blue-spectrum ALAN and prostate cancers when comparing the first and third tertiles of outdoor ALAN levels. Existing research has connected ALAN and other disruptors of the circadian rhythm to breast cancer. That being said, there is still little evidence linking ALAN to other tumours (Al-Naggar & Anil, 2016; Kloog, Stevens, Haim, & Portnov, 2010; Li et al., 2010; Rybnikova, Haim, & Portnov, 2015; Walker et al., 2020).

Conclusion:

Numerous critical processes in the development of cancer are regulated by circadian rhythms, and there is a clear negative relationship between circadian rhythms and cell proliferation. Disorders of the circadian rhythm impact oncogenesis. Clinical studies really reveal a substantial correlation between ALAN and breast cancer and a weak link between ALAN and other malignancies. There is strong evidence from rat studies that artificial evening illumination is a factor in the development of cancer. In summary, the available data supports a connection between ALAN and oncogenesis. There may be a number of strategies to decrease ALAN's carcinogenic effects, given our present understanding of ALAN and carcinogenesis: If you can't avoid evening lighting, turn off all of your lights for the night, use glasses that block short wavelengths of light, such as blue light, and get guidance if needed.

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