

Commentary

The Effect of Biological Clock & Molecular Clock in Cancer

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ABSTRACT

Nowadays change in lifestyle can most effect in our health, such as Insomnia & circadian rhythm changes. In this mini-review article, we focus on the circadian rhythm changes and cancer. Our study was shown to us, existence any changes in the circadian rhythm and biological clock leads to various changes in the levels of melatonin in the human body. Melatonin in Human cells, it is responsible for the adjustment of the circadian rhythm and produced in pineal glands. Disruption in levels of melatonin definitely related to cancers, such as ovary, uterus, prostate, endometrium, leukemia, breast cancer. Circadian rhythm controlled by 8 important and mainly genes that related to apoptosis, cell cycle, and checkpoint. Changes in this genes significantly related to cancers. Finally, these results are obtained that the change in the biological clock, causing a change in the molecular clock. Following the regular sleep pattern, a major role in human health.

Keywords: Biological Clock, Molecular Clock, Cancer, Circadian Rhythm.

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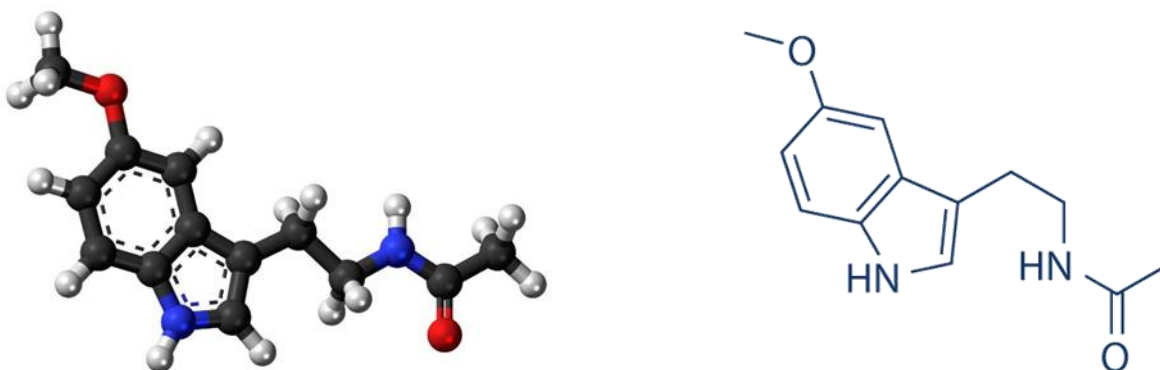
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The phenomena of Insomnia is widely found in the general population (1). But the more worrying issue is that it can lead to the incidence of or aggravate various health and psychiatric problems (2). Although the cardiovascular problems and the disorders of endocrine glands are some of the examples that are categorized in these cases (1-3) but the main concentrate of us in this review article is on the cancer disease (4). The existence of various

changes in the circadian clock and bio-clock leads to various changes in the levels of melatonin (5) an indoleamine molecule (N-acetyl methoxy tryptamine) or what we call it melatonin (Figure1). It exists widely in nature and can be found in plants, algae, bacterium, and human (6). But in human, it is responsible for the adjustment of the circadian rhythm (7).

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(Figure1: Melatonin Structure)

Although melatonin is produced in the most organs such as pineal gland, retina, lymphocytes, digestive system, and etc. but in mammals, it is mainly produced in pineal gland (8,9). Disruption of bio-clock leads to a significant reduction in the amount of melatonin (5). But, the significant role of melatonin in the issue of cancer become important when we find that the reduction in the level of melatonin causes the possibility of an increase in the development of cancer (5) such as ovary, uterus endometrium, prostate, leukemia (10), and especially breast cancer (5). Development of breast cancer is also possible through the production of estrogen and a change in the function of estrogen receptor (5). However, the studied field becomes more interesting when we find that the circadian rhythm is controlled

by around 8 main genes that each of these genes play a significant role in the very important cellular incidences such as cell cycle, checkpoint, and apoptosis (11,12). These genes are divided into 2 families: 1) *Period* and 2) *Cryptochrome*. In the mammals in the family of *Period*, there are 3 genes, *Per1*, *Per2*, and *Per3* and in the family of *Cryptochrome*, there are 2 genes, *Cry1* and *Cry2*, that the final product of them adjust the circadian rhythm by connection to a protein dimer (CLOCK/ BMAL1)(5,11,12). CLOCK and BMAL1 can control the cell cycle directly (7,11). The other genes that play a significant role in the circadian rhythm and on the other hand, are important in the cell cycle are named *Wee1* that transfer the cell cycle from the step G2 to the step M (11,12).

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Also, *c-Myc* that plays an important role in many of the cancers transfers the cell cycle from G0 to G1 and the role of Cyclin D1 is passing from step G1 to step S (11,13). The role of *c-Myc* has been proved in apoptosis and cellular proliferation (8,11,14). Destruction of the above cycle leads to the carcinogenesis phenomena and is considered as one of the reasons of cancer development (11,12,15).

Table 1. Ligands with corresponding cancerous cell surface specific antigens

Circadian Rhythm Controlled by 8 Important and Mainly Genes		
<i>Period</i>	<i>Per1</i>	
	<i>Per2</i>	
	<i>Per3</i>	
<i>Cryptochrome</i>	<i>Cry1</i>	That the final product of them adjust the circadian rhythm by connection to a protein dimer (CLOCK/BMAL1)
	<i>Cry2</i>	<i>CLOCK</i> and <i>BMAL1</i> can control the cell cycle directly
Another Important Gene	<i>Wee1</i>	that transfer the cell cycle from the step G2 to the step M
	<i>C-Myc</i>	The role of <i>c-Myc</i> has been proved in apoptosis and cellular Proliferation transfers the cell cycle from G0 to G1.
	Cyclin D1	the role of Cyclin D1 is passing from step G1 to step S

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Conclusion

Prevention is always better than treatment. In this review article, by studying the regular and apparently simple incidences that happens in our body routinely and adjusting the circadian rhythm and investigating their relation to cancer development, we have tried to simply provide a way to prevent cancer.