

Can a Disrupted Circadian Rhythm Cause Cancer?

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In our modern world, working late into the night or even starting a shift after the sun has gone down is not uncommon. The use of artificial light in our homes and electronics has led to more people reporting less sleep at night as well as irregular sleeping patterns. It is well known that, during sleep, our cells utilize the rest period to repair damaged cells and regenerate new cells after apoptosis (programmed cell death) of older cell bodies. Researchers are currently investigating the theory that due to modern sleep schedules, disrupted circadian rhythms could be a contributing factor to the rise of cancer in modern times. This theory stems from the idea that, without a normal circadian rhythm, cells are unable to move through their normal processes of repair and regeneration. This disruption could theoretically lead to higher concentrations of damaged or mutated cells, such as those that can cause cancer. Cells that evade apoptosis, those that are unable to be repaired from outside damages, or cells affected by mutations often are subject to changes in behavior which can result in the rapid cell division that can cause cancer. Suppose researchers could definitively prove the link between disrupted circadian rhythms and cancer-causing cells. In that case, there is a possibility that we could lower the chances of cancer in individuals who suffer from irregular sleep schedules by regulating their sleep cycles more efficiently.

Introduction

It has long been understood that our circadian rhythms regulate critical cycles in our body such as the sleep-wake cycle, the eating-fasting cycle, and the activity-rest cycle (Zhou et al. 2022). These cycles are regulated by interlocked transcription-translation feedback loops involving a variety of transcription factor proteins (Sulli et al. 2019). The function of these feedback loops is encrypted in 'clock genes' which can cause issues such as insomnia, immunity deficiencies, and some eating disorders if they are damaged or mutated. Even though these clock genes can affect immunity when mutated, immune-based drugs and therapies have little effect on curing their ailments in the body (Cash et al. 2021). This is because of the fact that they are involved in daily body functions and are not recognized as a threat by a person's immune system. It is now theorized that mutations in these genes could also lead to cancer as well. This is due to the growing evidence from recent research into the

effect that disrupted circadian rhythms have on tumorigenesis and their role in the facilitation of establishing cancer hallmarks (Sulli et al. 2019). Because of these recent discoveries, researchers are now looking into ways to use this evidence to improve knowledge of this life-threatening disease in people.

Recent Progress

Scientists and practitioners are now working towards ways to use this new information to improve many aspects of cancer research including prediction, prevention, diagnosis, treatment, and even recovery. A study that was completed in 2019 and posted in *Trends in Cancer* looks into the effect that a disrupted circadian rhythm has on tumorigenesis and the establishment of cancer hallmarks in cells (Sulli et al. 2019). This study looked into even further causes of these issues such as some oncogenic processes causing weakened circadian signaling and prevention options for such cases. It was proposed that pharmacological modulation of core clock

genes in patients prone to disrupted circadian rhythms could be a possible solution for the prevention and possibly even treatment of cancer and other related issues.

A more recent study published in the *Journal of Hematology & Oncology* explores the many different cycles affected by the circadian rhythm and how they could possibly interplay with cancer (Zhou et al. 2022). These researchers also proposed options for clock-related therapy for patients currently diagnosed with cancer to regulate the progression of tumor cells and hopefully stop or regress the growth of cancerous tumors in these patients. This treatment could theoretically also help the body begin to self-regulate and repair cells once it has returned to a normal circadian rhythm.

Another study, published online, is labeling circadian disruption as a cancer promoter (Cash et al. 2021). The manuscript states its main goal is to understand the relationships between circadian markers, cancer biology, and immunotherapeutics. This study brings up the question of how circadian signals play a role in tumor response to immune-based anti-cancer therapeutics such as T-cell therapy and checkpoint inhibitors.

Finally, a very interesting study was published recently in the journal *Science Advances* that puts all of these pieces together and states that their findings prove that disrupted circadian rhythms increase the risk of lung cancer, specifically (Pariollaud et al. 2022). This paper explains that when the circadian rhythm gets disrupted it implicates HSF1, a cancer signature gene, which can trigger lung tumors. This study also points out that due to how drastically the lungs are affected by the circadian rhythm, they seem to be particularly vulnerable when it becomes disrupted. Similar to the other studies cited, this paper presents the possibility of drug therapy to counteract this cause-and-effect scenario and prevent cancer in patients suffering from these disrupted rhythms.

Discussion

The idea that sleep cycles (in simple terms) could have such a devastating effect on the body is understandably a difficult concept to grasp. The science behind circadian rhythms, however, proves that this could very well be a possibility. Research that has been done based on this theory has further proved that disrupted circadian rhythms can have large effects on the human body and for good reason. Our circadian rhythms regulate so many important processes in our body such as rest, activity, sleep, and appetite. These processes are critical for many functions of our brain and body. Sleep in particular has been found to be a huge component in the life cycle of cells throughout our body as well as a regulator for immune responses, apoptosis, cell health, and regeneration. The transcription factor proteins that signal these cycles are all

controlled by clock genes, which makes it essential that these genes are functioning properly. Any damages or mutations in these genes can not only cause harm to any of these cycles but could possibly cause a change in cell behavior leading to a cancerous cell growth as it can in any other mutated gene. The fact that these genes already code for cell growth, death, and recognition means that a mutation such as this is very possible and could easily lead to cancerous cells as well as aid in tumorigenesis.

One trend that was seen in each study is that tumor growth and circadian signals did have a consistent effect on one another; if a tumor formed the symptoms would often be lack of sleep, loss of appetite, and loss of energy. On the other hand, if the circadian rhythm was significantly and repeatedly disrupted to the point of loss of function, the risk of tumor growth rose significantly.

The idea of using medication to control these clock genes in hopes of controlling this connection between circadian signals and cancerous cell growth is interesting as well. Boosting these processes that are signaled by the circadian rhythm would basically allow the body to improve on its own much like any immunotherapy drug or treatment. Medical therapies that are able to maximize the benefits of the circadian signals and processes, could also work in the prevention of cancer in those prone to the disease as well as help those with other disorders caused by a circadian rhythm imbalance. These may include sleep disorders, eating disorders, immune disorders, and even neurological and cardiovascular diseases.

Each study made a larger point quite clear: the circadian rhythm has an effect on many different tissues in our body and has a large impact on many of the essential processes that we must have functioning to survive. Even though many of these studies used model organisms in their experiments, this information is still relative to any organism that can see the sun and can get cancer, of which, there are countless. New realizations lead to new research that will eventually lead to new improvements in our daily lives and understanding. New treatments will always take a while to improve but if this connection between our natural circadian rhythm and a random cancerous growth can be harnessed by researchers and practitioners, it may mean a large improvement in many fields of medicine in the future, as well as help and relief for millions of people.

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