Medication timing key in cancer treatment

• **Achievements** [1]

An internal clock determines many of our bodily functions. The same is true for tumour cells, EU-funded research suggests. This discovery could point the way to a more efficient, personalised approach to cancer treatment.

The biological clock located in our brain regulates hundreds of biochemical, physiological and behavioural processes that rhythmically oscillate in our body throughout the day. These 24-hour circadian rhythms are found, in mammals, in virtually every individual cell in the body. Every day circadian rhythms are synchronised to the outside world, and daylight is one of the most important synchronisers.

There are circadian rhythms in many aspects of disease as well. The intensity of signs and symptoms rhythmically changes in the course of the 24-hour day. The same is true of our body's receptiveness to medication. Here is where the concept of chronotherapy - the application of treatment at the most optimal time of day to increase therapy success - comes into play.

**The right timing**

“During the last 30 years, the potential of using chronotherapy to improve the efficacy of anticancer therapy has been demonstrated,” says Maria Comas Soberats, the beneficiary of the EU-funded
CANCERTIME research grant. Thanks to CANCERTIME, she was able to spend two years at the Roswell Cancer Institute in Buffalo (USA), and one year at the Department of Microbiology, Tumor and Cell Biology of the Karolinska Institute in Stockholm (Sweden), one of Europe’s leading medical research institutes.

So far, few hospitals have taken advantage of the benefits of chronotherapy. This is partly because the best time to apply many types of treatment is during the night when there is lack of infrastructure and personnel. In addition, little is known about the mechanisms that relate specific cancer treatments with the circadian clock.

'Guardian of the genome'

“If we can understand how daily patterns of toxicity and sensitivity to cancer treatment vary throughout the day and how chronotherapy functions at the cellular level for each type of treatment, this should stimulate novel approaches for treating the disease,” explains Comas Soberats. “In this project, we have done this type of studies for several potential anticancer drugs that target the p53 protein which has been described as ‘the guardian of the genome’.”

The p53 protein regulates the cell cycle in multicellular organisms such as animals and humans. It plays a central role as a tumour suppressor, preventing genome mutation and thus cancer. In the framework of CANCERTIME, Comas Soberats found that there is a link between p53 and the circadian clock. She and her colleagues tested several drugs that target the p53 protein and could be candidates as chronotherapy targets.

In addition, Comas Soberats discovered that all of the tumour types investigated during CANCERTIME retain a functional clock that is synchronised with the surrounding tissue.

The clock is ticking for cancer

Kept alive in a petri dish, these tumours can even continue to oscillate for several days once they have been removed from the body. This confirms that the circadian clocks in these tumours can keep working even when they do not receive hormonal or metabolic signals from surrounding tissue. This knowledge will help design chronotherapy strategies for cancer patients.

As a result, anticancer therapy will become personalised over the coming years: doctors will take a sample of each tumour and will determine its specific genetic characteristics. In combination with more information from that specific patient, they will be able to design a personalised treatment that will provide the highest chance of success for that individual.

Every individual has a specific chronotype, depending on what time of the day their physical functions (hormone levels, cognitive faculties and sleep, for example) change or reach a certain level. Both the patient’s chronotype and a chronotherapeutic approach should be taken into consideration in the personalised treatment of cancer, concludes Comas Soberats.

Cancer chronotherapy. Timing each type of treatment to its most optimal time of the day or night increases chances of success.

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