

# The biological clock as an ally in the fight against inflammatory disease

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What if the symptoms and seriousness of certain inflammatory diseases were linked to time of day? Researchers from Inserm, Institut Pasteur de Lille and Université de Lille have been working on this hypothesis, after noting that the seriousness and mortality associated with fulminant hepatitis were dependent on the time at which the disease was induced. Their study, conducted on human cells and mice, shows that the anti-inflammatory action of a biological clock protein could prevent the onset of fulminant hepatitis by alleviating symptoms and increasing survival rates.

This research has been published in *Gastroenterology*.

Fulminant hepatitis is a serious disease that leads to rapid deterioration of tissue and liver function associated with blood coagulation disorders and irreparable brain damage. Overdose with medications containing acetaminophen is among the most common causes of the disease. Accumulation of acetaminophen in the body can cause cellular stress, which gives rise to an abnormal immune system response. This is expressed by excessive inflammation, which destroys hepatocytes and the liver. Until now, no specific treatment for fulminant hepatitis has been identified, and the only solution is liver transplant within 24 hours following onset of symptoms. Researchers from Inserm, Institut Pasteur de Lille and Université de Lille are focusing on the mechanisms underlying inflammation specifically in fulminant hepatitis, with a view to identifying potential avenues of treatment.

Starting from the observation that immune functions vary during the day, the researchers examined a biological clock protein called Rev-erb $\alpha$  and its potential role in regulating inflammation in fulminant hepatitis. This protein notably targets adipose tissue, together with liver, skeletal muscle and brain cells. It plays a major role in developing and regulating the circadian rhythm, i.e. the repetition of the biological cycle every 24 hours.

This new research, conducted on human immune system cells and on mice, showed that the inflammation also follows a circadian rhythm. The researchers observed that injecting a molecule potentiating the action of Rev-erb $\alpha$  reduced the inflammatory response causing hepatocyte death in fulminant hepatitis. Mice having received the Rev-erb $\alpha$ -activating treatment demonstrated less severe forms of the disease, and had a higher survival rate. As the same results were observed in vitro on [human cells](#), these data indicate new avenues to be explored with a view to potentially developing a treatment for acute fulminant hepatitis, and slowing the progression of symptoms in patients awaiting transplantation.

Fulminant [hepatitis](#) is not the only disease involving the circadian molecular mechanism inhibited by Rev-erb $\alpha$ . Other diseases such as peritonitis, diabetes or even atherosclerosis display a similar imbalance in the [inflammatory response](#) due to the abnormal accumulation of toxins in the body. Inserm researcher H el ene Duez says, "The results of this study could open up new prospects in preventing these diseases. They also offer new avenues for researchers, notably in terms of potential improvements in quality of life and longevity among patients suffering from [chronic inflammatory disease](#)."

**More information:** B. Pourcet et al, Nuclear Receptor Subfamily 1 Group D Member 1 Regulates Circadian Activity Of NLRP3 Inflammasome to Reduce the Severity of Fulminant Hepatitis in Mice,

*Gastroenterology* (2017). [DOI: 10.1053/j.gastro.2017.12.019](https://doi.org/10.1053/j.gastro.2017.12.019)

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