

When body clock runs down, immune system takes time off

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It's been said that timing is everything, and that may be particularly true when it comes to the ability to fight off disease. New research published by Cell Press in the February issue of the journal *Immunity* shows that the success of host immune defense depends in part on an organism's "body clock." The study may lead to therapeutic strategies designed to optimize the immune response and to protect patients at the time when they are most vulnerable.

Many organisms have evolved an endogenous timing system called a [circadian clock](#) that regulates a wide variety of metabolic activities over a twenty-four hour cycle. "It is becoming increasingly evident that disruption of daily rhythms, such as from sleep deprivation, affects the immune response," explains senior study author, Dr. Erol Fikrig from Yale University School of Medicine. "In our study, we were interested in investigating whether the ability of the immune system to detect a pathogen is under circadian control and whether there are timing-associated consequences for the subsequent immune response."

Dr. Fikrig and colleagues examined the expression and function of Toll-like receptor 9 (TLR9), an [immune system protein](#) that can sense bacterial and [viral DNA](#). The researchers demonstrated that the circadian clock controlled TLR9 expression and function and that mice immunized when TLR9 was most responsive exhibited an enhanced immune response. Importantly, in a mouse model of sepsis, [disease severity](#) was dependent on the timing of sepsis induction, which directly correlated with cyclical changes in TLR9. The authors suggest that this

observation may be clinically significant as septic human patients are known to be at increased risk of mortality between 2 and 6 am.

"These findings not only unveil a novel, direct molecular link between [circadian rhythms](#) and the immune system, but also open a new paradigm in the biology of the overall immune response with important implications for the prevention and treatment of disease," concludes Dr. Fikrig. "Furthermore, patients in the ICU often have disturbed sleep patterns, due to noise, nocturnal light exposure and medications; it will be important to investigate how these factors influence TLR9 expression levels and immune responses."

More information: Silver et al.: "The circadian clock controls toll-like receptor 9-mediated innate and adaptive immunity."

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