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*Clinical Significance of Circadian Rhythms Disruption in Sjögren's Pathogenesis*

## LAY ABSTRACT

The Lay Abstract is for publicity purposes and should use simple language summarizing the proposed research and its significance.

The circadian clock is an endogenous mechanism that regulates our body's functions such as sleep/wake status, saliva flow, metabolism, and hormone release. Several autoimmune diseases are caused, at least in part, by malfunction of circadian clocks. Our aim is to achieve a better understanding of the causes that result in Sjögren syndrome (SS), the second most common autoimmune rheumatic disease in the US, in which immune cells attack and destroy the glands that produce saliva and tears. SS patients suffer greatly by the lack of saliva (dry mouth) and tears (dry eye) and the current therapeutic options are not satisfactory. We found that in patients with SS the salivary gland circadian clock does not work properly. We propose to study how changes in our circadian clock initiate and/or control progression of SS. Our goal is to provide foundation for better diagnostic markers and novel treatment modalities for these patients.

## SCIENTIFIC ABSTRACT

The Scientific Abstract is written for SSF reviewers and a professional audience.

Circadian rhythms are endogenous self-sustained oscillations with 24h periods that regulate diverse physiological processes through complex gene regulation orchestrated by "clock" transcription factors. Disruption of circadian rhythms deregulates cell proliferation, inflammation and immunity response, resulting in significantly increased risk for autoimmune diseases. We recently demonstrated the existence of a salivary gland circadian clock that regulates saliva flow. We also discovered that the salivary circadian clock is severely impaired in patients with SS, suggesting that alterations in this clock may contribute to disease pathogenesis. We hypothesize that the circadian clock directly contributes to the initiation and/or progression of SS. Our aim is to identify direct correlations between melatonin levels (an indicator of circadian functions) and diminished saliva flow, sleep patterns/fatigue, and disease activity in SS patients. Functional studies using clock mutant mice and drugs resetting the circadian clock will provide insights on the mechanism linking the circadian clock and SS.