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Clock-dependent chromatin topology modulates circadian transcription and behavior

Jérôme Mermet[1,4], Jake Yeung[1,4], Clémence Hurni[1], Daniel Mauvoisin[1], Kyle Gustafson[1], Céline Jouffe[2], Damien Nicolas[1], Yann Emmenegger[3], Cédric Gobet[1,2], Paul Franken[3], Frédéric Gachon[1,2] and Félix Naef[1]

[+] Author Affiliations

Corresponding author: felix.naef@epfl.ch

[4] These authors contributed equally to this work.

Abstract

The circadian clock in animals orchestrates widespread oscillatory gene expression programs, which underlie 24-h rhythms in behavior and physiology. Several studies have shown the possible roles of transcription factors and chromatin marks in controlling cyclic gene expression. However, how daily active enhancers modulate rhythmic gene transcription in mammalian tissues is not known. Using circular chromosome conformation capture (4C) combined with sequencing (4C-seq), we discovered oscillatory promoter–enhancer interactions along the 24-h cycle in the mouse liver and kidney. Rhythms in chromatin interactions were abolished in arrhythmic *Bmal1* knockout mice. Deleting a contacted intronic enhancer element in the *Cryptochrome 1* (*Cry1*) gene was sufficient to compromise the rhythmic chromatin contacts in tissues. Moreover, the deletion reduced the daily dynamics of *Cry1* transcriptional burst frequency and, remarkably, shortened the circadian period of locomotor activity rhythms. Our results establish oscillating and clock-controlled promoter–enhancer looping as a regulatory layer underlying circadian transcription and behavior.

Keywords

circadian rhythms chromatin topology promoter–enhancer loops DNA regulatory elements transcriptional bursting

Footnotes

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