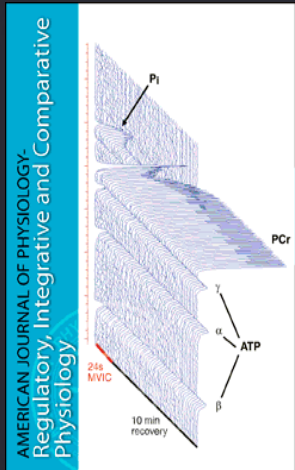




Details



American Journal of Physiology-
Regulatory, Integrative and
Comparative Physiology

Volume 304, Issue 12

Jun 2013

Pages R1053-R1182

ARTICLE

Mechanism of the circadian clock in physiology

[View article page](#)

Jacob Richards and Michelle L. Gumz

” CITE

Copyright © 2013 the American Physiological Society
<https://doi.org/10.1152/ajpregu.00066.2013>

Publisher American Physiological Society

ISSN 0363-6119

eISSN 1522-1490

Online April 10, 2013

Print June 15, 2013

Accepted April 9, 2013

Received February 1, 2013

Pages R1053 - R1064

Am J Physiol Regul Integr Comp Physiol 304: R1053–R1064, 2013.
First published April 10, 2013; doi:10.1152/ajpregu.00066.2013.

Review

EB 2012 | Mechanism of the Circadian Clock in Physiology

Mechanism of the circadian clock in physiology

Jacob Richards^{1,2} and Michelle L. Gumz^{1,2}

¹Department of Medicine and ²Department of Biochemistry and Molecular Biology, University of Florida, Gainesville, Florida

Submitted 1 February 2013; accepted in final form 9 April 2013

Richards J, Gumz ML. Mechanism of the circadian clock in physiology. *Am J Physiol Regul Integr Comp Physiol* 304: R1053–R1064, 2013. First published April 10, 2013; doi:10.1152/ajpregu.00066.2013.—It has been well established that the circadian clock plays a crucial role in the regulation of almost every physiological process. It also plays a critical role in pathophysiological states including those of obesity and diabetes. Recent evidence has highlighted the potential for targeting the circadian clock as a potential drug target. New studies have also demonstrated the existence of “clock-independent effects” of the circadian proteins, leading to exciting new avenues of research in the circadian clock field in physiology. The goal of this review is to provide an introduction to and overview of the circadian clock in physiology, including mechanisms, targets, and role in disease states. The role of the circadian clocks in the regulation of the cardiovascular system, renal function, metabolism, the endocrine system, immune, and reproductive systems will be discussed.

circadian; clock; metabolism; cardiovascular; immune; endocrine; renal; diabetes; obesity

THE CONCEPT OF CIRCADIAN RHYTHMS was first documented in the 18th century, when the French astronomer de Mairan recorded his observation that the opening and closing of heliotrope plant leaves occurred independently of sunlight (65). Now it is apparent that almost all facets of physiology display rhythmic oscillations from the simplest archaeobacteria to humans (79); these rhythms are controlled by an internal circadian clock. The purpose of this review is to provide an overview of the role the circadian clock plays in the regulation of a variety of mammalian physiological functions.

promoters of target genes, which drive the positive transcription arm of the TTO loop. Two of these target genes encode the circadian proteins Period (Per) (homologs: 1, 2, and 3) and Cryptochrome (Cry) (homologs: 1 and 2). These two proteins interact, translocate into the nucleus, and inhibit the activity of CLOCK and BMAL1, which promotes the transcriptional repression arm of the TTO loop. Other accessory proteins include D-site albumin binding protein (DBP), and the nuclear orphan receptors retinoid-related orphan receptor (ROR) and REV-ERB, which modulate the activity of the loop through activation (ROR) or