P-27

Cyclic and Differential Expression of Clock Genes *In Vivo* and *In Vitro*

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Many biological systems are regulated by an intricate set of feedback loops that oscillate with a circadian rhythmicity of roughly 24 hr. For example, increases in body temperature, heart rate, blood pressure, and cortisol secretion occur early in the day. Cardiovascular diseases also manifest diurnal variation. Heart attacks and stroke are more common in the early morning. A master clock that controls circadian rhythms is located in the suprachiasmatic nuclei of the hypothalamus. Peripheral clocks have also been demonstrated in most major organs, including the heart, where several genes involved in the regulation of circadian rhythm are expressed, such as *clock*, *bmal1*, *cry1*, *cry2*, *per1*, *per2*, and *per3*. In addition to these circadian regulators of transcription, many other genes also cycle, including metabolic and stress-related genes. Numerous aspects of cardiovascular physiology and pathology vary during the 24-hour day. Yet, mechanisms regulating intrinsic rhythmicity of cardiac gene expression are poorly understood. The "master clock" located within the suprachiasmatic nucleus of the hypothalamus can be "set" by light stimulation. We hypothesized that environmental stress can similarly regulate circadian gene expression in the heart. Real-time RT-PCR measurements in a cardiomyoblast cell line (H9c2) documented diurnal variation in the activation of "clock" genes *bmal1* and *per2*. Modest rhythmicity was detected for *clock* under basal conditions, but serum shock induced robust rhythmic expression. Diurnal variation of clock gene expression in the heart is altered by biome-

chanical stress, suggesting a role in anticipating and responding to environmental stimuli.

Key words) *Circadian rhythm, Diurnal variation, Cardiomyoblast cell line (H9c2), Biological clock, Environmental stress*

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