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Circadian Mechanisms in Medicine

Hugo Y.-H. Lin, M.D., Ph.D.,

Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

Ming-Yu Yang, Ph.D.,

Chang Gung University, Tao-Yuan, Taiwan

Sheng-Fung Lin, M.D.

E-Da Hospital, Kaohsiung, Taiwan

To the Editor:

Allada and Bass (Feb. 11 issue)¹ provide a comprehensive review of circadian mechanisms in medicine, focusing on physiology, molecular circuitry, and the contribution of circadian processes to disease. Although circadian misalignment causes disease, epigenetic modifications of circadian gene expression are also influential and usually involve DNA methylation at CpG sites (locations in DNA at which a cytosine precedes a guanosine in the 5' to 3' sequence).²⁻⁴ DNA methylation plays a crucial role in embryonic development and across the human lifespan, including the recovery of persons with circadian disorders.⁴ However, according to our previous research,⁵ methylation is not temporary. Methylated CpG sites are prominent in patients with chronic myeloid leukemia (CML). The treatment of patients with CML could reactivate JUNB, an activating protein 1 transcription factor that is important in the control of cell growth and differentiation and neoplastic transformation. Epigenetic modifications of circadian genes should be viewed as central to certain disease processes.

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hugoyl@kmu.edu.tw .

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