



## “Nobel” Clock: Deeper Impact than We Originally Thought!

S. R. Pandi-Perumal<sup>1</sup> · Ravi Gupta<sup>2</sup>

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It is a golden period for sleep researchers as the Nobel Prize for Medicine in 2017 was awarded jointly to Jeffrey C. Hall, Michael Rosbash, and Michael W. Young “for their discoveries of molecular mechanisms controlling the circadian rhythm”. This recognition will definitely be helpful to “wake-up” the world regarding the impact of sleep on health. By now we have sufficient literature to suggest that the quality, and quantity, as well as the timing of sleep are important factors for a healthy life and a necessary ingredient for a good night sleep.

A lot of literature is available to suggest that sleep duration has a profound impact on body physiology. Sleep deprivation, as well as altered sleep duration, have been found to pave way for cardiometabolic disorders, obesity, diabetes mellitus, stroke, cancer and finally premature death [1, 2]. Sleep deprivation and insomnia have been linked with hypertension and depression, while the impact of long sleep duration on these disorders is less clear [2, 3]. Poor sleep quality, as well as disturbed sleep duration, correlates with subclinical cardiovascular disease [4]. However, in the modern world sleep timing has become a more important issue, which has two-way interaction with the circadian clock.

The circadian clock is not unique to humans, rather, it has been found among all living species, from Cyanobacteria to Angiosperms and from Protozoa to Mammals, including *Homo sapiens*. This timing mechanism is an oscillator that orchestrates a variety of circadian outputs in diverse processes, ranging from gene expression to physiology and behavior of an organism [5, 6]. Sleep has been considered as a biological rhythm. There are several sleep disorders that are related to the dysregulation of circadian rhythm. For

example, advanced sleep phase syndrome (ASPS), delayed sleep phase syndrome (DSPS), non-24-h sleep–wake disorder, irregular sleep–wake syndrome, jet lag, and shift work disorders [7].

With technological and industrial development we are living in a world that is working 24 h and 7 days a week. Such huge demands are met by curtailing and altering the timing of the sleep. Playing with the sleep to meet the demands of modern world has come with a price. Many people who have frequently changing working hours develop shift work disorder that has a negative impact on work performance manifested as errors, accidents to health consequences ranging from memory changes to certain cancers, especially that of breast and prostate [8].

Discovery of molecular mechanisms underpinning the circadian clock by Hall, Rosbash, and Young has paved way for understanding the physiology of various body functions as well as that of disorders at the molecular level. From the cradle to grave, this circadian clock plays a pivotal role in diverse biological functions. In healthy individuals, the circadian rhythms exhibit normal endogenous circadian rhythms. Disruption of these rhythms has an adverse effect on human physical and mental health including affect, behavior, and cognition [9–12]. It is well known that several medical and mental conditions show dysregulation of circadian rhythms and sleep/wake cycle [13]. For example, loss of circadian rhythm in the expression of BMAL-1 has been found to impair locomotor activity and altered temperature regulation [14]. Expression of these genes is governed by sleep–wake schedule as rotating shift work has been found to negatively influence methylation of PER1, PER2 and BMAL-1 genes in dose-dependent manner [15]. However, duration of sleep, as well as chronotype, also influence the methylation of genes involved in circadian clock [16]. Altered expression of genes of circadian clock has been found to correlate with disorders. For example, Per1, Per2, and Clock expression govern the size and depth of invasion of colorectal carcinomas [17].

Despite mounting evidence, the use of chronotherapy is still in its infancy. This includes the use of light therapy,

✉ Ravi Gupta  
sleepdoc.ravi@gmail.com

S. R. Pandi-Perumal  
pandiperumal2017@gmail.com

<sup>1</sup> Somnogen Inc., Toronto, Canada

<sup>2</sup> Department of Psychiatry and Sleep Clinic, Himalayan Institute of Medical Sciences, Dehradun, India

wake therapy, dark therapy, and the use of chronobiotics such as melatonin. A renewed interest and wider acceptance are expected in the coming years. Employing a multidisciplinary and translational or the bench to bedside approach including chronotherapeutic modalities would benefit the masses in the years to come.

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