Expression Dynamics In A Cell Line Derived From Rat Supurachiasmatic Nucleus

Hajime Tei
Mitsubishi Kagaku Institute of Life Sciences

Many biochemical, physiological and behavioral processes in many organisms exhibit circadian rhythms. Circadian rhythms are driven by autonomous oscillators and entrained by daily light-dark cycles. In fact, the suprachiasmatic nucleus (SCN) in the hypothalamus of brain is a dominant circadian pacemaker in mammals, and necessary for most behavioral and physiological rhythms. Environmental cues such as light-dark cycles are transmitted through a specific neuronal pathway from eyes to the SCN, and the SCN can entrain the peripheral circadian rhythms.

The transcription of Per1, a mammalian clock gene, oscillates in the suprachiasmatic nucleus and peripheral tissues (liver, muscle, and lung) with a tissue specific manner, indicating that the oscillation of Per1 can be utilized as a molecular marker of ticking circadian clocks in both cells. Then we constructed transgenic rat lines with a Per1::luc reporter gene. The expression of luciferase is under the control of the Per1 promoter in the tissues of the transgenic rat lines. Light emission from the cultured SCN of these rats was robustly rhythmic for up to 30 days in vitro. However, cultured liver, lung and skeletal muscle tissues expressed circadian rhythms that damped after 2-6 cycles. To elucidate the specific properties the mammalian master clock (SCN), we established neuronal cell lines derived from the embryonic SCN of the Per1::luc transgenic rat. The Per1 expression in these cell lines exhibited an autonomous oscillation, and phase shifted (advanced and delayed) after forskolin stimulation in a time-dependent manner. We analyzed the time courses of the expression patterns of the cell line using affymetrix genechip technology. We revealed that the transcription of appropriately 663 genes (4.1%) with functional groups covering a broad spectrum of cellular pathways was regulated by circadian clock. In addition, the expression dynamics during phase shift of the cell line will be discussed further.