An ecdysone-responsive nuclear receptor impacts circadian rhythms in Drosophila

Shailesh Kumar[1], Dechun Chen[1], Christopher Jang[1], Alexandra Nall[1], Xiangzhong Zheng[1] and Amita Sehgal[1,2]

[1]Department of Neuroscience, [2]Howard Hughes Medical Institute, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA 19104

Summary

Both circadian clocks and steroid hormone signaling are important for normal physiology, but little is known about molecular links between these processes. Through a gain-of-function screen for novel circadian rhythm genes, we identified a circadian function for a nuclear receptor, Ecdysone Induced Protein 75 (Eip75 or E75) that is induced by steroid signaling. We found that overexpression or knockdown of the E75 gene in clock neurons disrupts rest:activity rhythms and dampens oscillations of the PERIOD (PER) protein. Effects of E75 on the circadian clock are mediated in part through its direct repression of the gene encoding the transcriptional activator, CLOCK (CLK). Furthermore, we found that PER inhibits the activity of E75 on the Clk promoter, thereby providing a mechanism for a previously proposed de-repressor effect of PER on Clk transcription. The ecdysone receptor, upstream of E75 signaling, is also expressed in central clock cells and manipulations of its expression levels are similar to the effects of E75 on circadian rhythms. We find that E75 allows maintenance of rhythms under stressful conditions (nutritional and temperature), suggesting an important function for steroid signaling in the maintenance of circadian rhythms.

Trainee Award Eligible