Analysis of using feedback loops to explain the circadian oscillator in drosophil...

Science, Biology

Using feedback loops to explain the circadian oscillator in Drosophila

Introduction The report is about a study that was conducted to investigate how different models explain how the PER-TIM activation of dClk mRNA occurs in Drosophila. It is known that the circadian clock in Drosophila is controlled by five different genes: period (per), timeless (tim), double-tim (dbt), Drosophila Clock (dClk) and Cycle (Cyc). Of the five genes, per, tim and dClk are routinely expressed.

The highest quantities of dClk mRNA are synthesized very late at night and also in the early hours of the morning, while the highest quantities of per and tim mRNA are synthesized in the early hours of the evening. However, there is a considerable delay between when the peak levels of the per and tim mRNA are synthesized and when per and tim levels reach peak production late in the evening. The reason for this is the phosphorylation that destabilizes the PER, causing it to undergo dimerization with TIM. This occurs in the nucleus.

There is little that is known with regards to how dClk mRNA is regulated. Previous studies have found low quantities of dClk mRNA in Drosophila that do not have functioning PER and TIM, indicating that PER and TIM are also responsible for activating dClk.

Study and results

This study involved measuring the levels of dClk mRNA levels in various mutant gene combinations. The results showed that the mutant genes did not display highly varying quantities of dClk mRNA over the circadian clock (Glossop, Lyons and Hardin).

The lack of dClk-dependent-PER alongside the relatively high levels of dClk

mRNA proves that PER-dependent dClk is not activated by localization of an activator in the nucleus. mRNA quantities in the dClk mutants were measured to prove that the activation of dClk was not as a result of PER-TIM dimmers being formed due to low quantities of per and tim in dClk mutants. Results from this measurement found that the levels of dClk mRNA were almost similar to the peak level of dClk mRNA found in wild flies, proving that dClk is activated by PER-TIM via derepression.

The negative feedback loop can be used to explain the observations made above. In this, the formation of PER-TIM dimers leads to sequestering of dCLK-CYC dimers that in turn hinder the CLK-CYC from functioning properly. This ultimately causes the derepression of dClk transcription.

The reduction of PER-TIM quantities in the early hours of the morning causes dimerization of dCLK-CYC. These dimers cause repression of dClk, resulting in a reduction of dClk mRNA levels by the time the day ends. This occurs along with the increase in the quantities of per and tim mRNA. In the evening, the reducing quantities of dClk mRNA occurs with the reduction of dCLK-CYC quantities resulting in a reduction in the transcription of per and tim and an increase in dClk mRNA buildup. This cycle is then repeated again when the quantities of PER and TIM in the nucleus increases.

Conclusion:

The results obtained from the study proved that the per-tim mechanism is responsible for the dClk circadian loop in Drosophila.

Reference:

Glossop, N. R., L. C. Lyons and P. E. Hardin. " Interlocked feedback loops within the Drosophila circadian oscillator." Science 22 October 1999: 766.