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The **circadian clock** is maintained by daily fluctuations in the Period and Timeless proteins that negatively regulate the transcription of their own genes. In the November 14 *Nature*, Grima *et al.* describe the mechanism responsible for the phosphorylation-dependent control of Period and Timeless protein degradation in *Drosophila* (*Nature* 2002, **420**:178-182). Investigation of components of the SCF-mediated ubiquitin proteasome pathway led to the identification of the Slimb protein as an essential cog in the clock within the fly's brain. The *Drosophila* **Slimb** gene (*Slmb*) encodes an F-box/WD40 protein that regulates the levels of different transcription factors. Rescuing the developmental lethality associated with *Slmb* mutation revealed that adult *Slmb* mutants were completely arrhythmic under conditions of constant darkness: Period and Timeless oscillations are abolished in constant darkness in the *Slmb* mutants, and hyperphosphorylated Period protein accumulates. This is the first characterized example of a proteasome degradation protein that regulates the circadian clock.

References

1. Stopping time: the genetics of fly and mouse circadian clocks.
2. *Nature*, [<http://www.nature.com>]
3. Regulation of the Hedgehog and Wingless signalling pathways by the F-box/WD40-repeat protein Slimb.