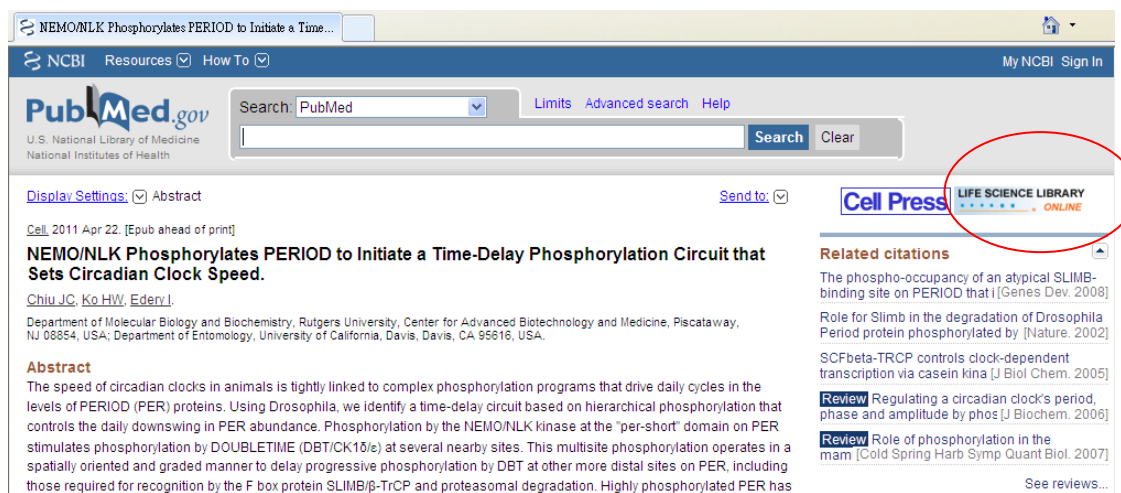


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NEMO/NLK Phosphorylates PERIOD to Initiate a Time-Delay Phosphorylation Circuit that Sets Circadian Clock Speed.

Chiu J.C., Ko H.W., Edery I.

Department of Molecular Biology and Biochemistry, Rutgers University, Center for Advanced Biotechnology and Medicine, Piscataway, NJ 08854, USA; Department of Entomology, University of California, Davis, Davis, CA 95616, USA.

Abstract

The speed of circadian clocks in animals is tightly linked to complex phosphorylation programs that drive daily cycles in the levels of PERIOD (PER) proteins. Using *Drosophila*, we identify a time-delay circuit based on hierarchical phosphorylation that controls the daily downswing in PER abundance. Phosphorylation by the NEMO/NLK kinase at the "per-short" domain on PER stimulates phosphorylation by DOUBLETIME (DBT/CK1 ϵ) at several nearby sites. This multisite phosphorylation operates in a spatially oriented and graded manner to delay progressive phosphorylation by DBT at other more distal sites on PER, including those required for recognition by the F box protein SLIMB β -TrCP and proteasomal degradation. Highly phosphorylated PER has

Related citations

- The phospho-occupancy of an atypical SLIMB-binding site on PERIOD that i [Genes Dev. 2008]
- Role for Slimb in the degradation of *Drosophila* Period protein phosphorylated by [Nature. 2002]
- SCFbeta-TRCP controls clock-dependent transcription via casein kina [J Biol Chem. 2005]
- Review** Regulating a circadian clock's period, phase and amplitude by phos [J Biochem. 2006]
- Review** Role of phosphorylation in the mam [Cold Spring Harb Symp Quant Biol. 2007]

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