

This Week in The Journal

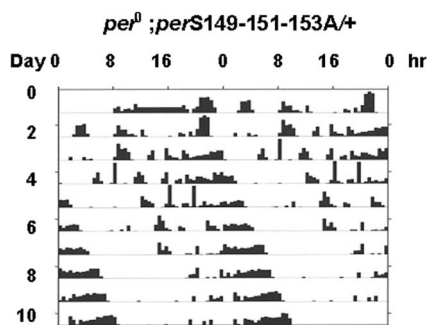
● Cellular/Molecular

Phosphorylating a Clock

Jui-Ming Lin, Analyne Schroeder, and Ravi Allada

(see pages 11175–11183)

Protein phosphorylation keeps circadian clocks wound, triggering rhythmic transcriptional events throughout the day. This week, Lin et al. identify phosphorylation sites on the *Drosophila* circadian protein PERIOD (PER). Mutations in casein kinase 2 (CK2) result in abnormal circadian phenotypes and altered PER nuclear localization, and CK2 specifically phosphorylates PER *in vitro*. The authors focused on three CK2 consensus sites on the N-terminal segment of PER, consisting of S/T-X-X-D/E amino acid sequences, two of which appeared to be responsible for CK2 phosphorylation *in vitro*. They then made alanine mutations of each site and looked at their effect on circadian function. Single, double, and triple mutations caused period lengthening. In *perS149-151-153A* triple mutants, PER localized to the nuclei of a ventral group of lateral pacemaker neurons ~2 h later than in wild-type flies. The authors propose that nuclear entry of PER is triggered by CK2 phosphorylation and contributes to period regulation.



Transgenic *perS149-151-153A* mutant flies were entrained on a 12 h light/dark cycle, and subsequently maintained in constant darkness for circadian locomotor analysis. See the article by Lin et al. for details.

▲ Development/Plasticity/Repair

EGFR and Migration of Neural Progenitors

Adan Aguirre, Tilat A. Rizvi, Nancy Ratner, and Vittorio Gallo

(see pages 11092–11106)

Postnatal neural progenitors must not only proliferate, they then must migrate. This week Aguirre et al. examine a signaling molecule, the epidermal growth factor receptor (EGFR) that appears to be important for the migratory step. The authors examined progenitors that express the proteoglycan NG2. NG2⁺ cells in the subventricular zone (SVZ) are highly proliferative and migratory, whereas NG2⁺ cells in the cerebral cortex and olfactory bulb divide slowly and are nonmigratory. The authors report that NG2⁺ cells in the SVZ, subcortical white matter, and rostral migratory stream expressed NG2 and EGFR, whereas NG2⁺ cortical cells had only low levels of EGF and EGFR. NG2⁺ cortical cells transfected with EGFR, or NG2⁺ cells from a transgenic mouse that constitutively expressed human EGFR, were transplanted into the lateral ventricle of wild-type mice. These cells migrated like wild-type NG2⁺ cells of the SVZ. Thus, enhanced EGFR expression gave them the gift of migration.

■ Behavioral/Systems/Cognitive

Monkey Amygdala Neurons and Reward Schedules

Yasuko Sugase-Miyamoto and Barry J. Richmond

(see pages 11071–11083)

The amygdala provides emotional context for outside events. In this week's *Journal*, Sugase-Miyamoto and Richmond recorded from single neurons of the basolateral complex while monkeys used visual cues to predict how much work was needed to obtain a reward. In the "reward schedule" task, monkeys were trained to release a button within a specified time window after a stimulus color change. The

brightness of the stimulus also contained information about how many more trials would occur before the reward. Most neurons responded with some specificity for bits of information contained in a trial, such as the schedule length, how many more trials would occur before the reward, or to the reward itself. When more trials were required, the monkeys' error rate and reaction time increased, an indication of reduced motivation. The amygdala thus provides information about the task to connected areas including the perirhinal, inferotemporal, and cingulate cortices that could influence emotional and motivational states.

◆ Neurobiology of Disease

Soluble A β and Degradation of Excitatory Synapses

F. Roselli, M. Tirard, J. Lu, P. Hutzler, P. Lamberti, P. Livrea, M. Morabito, and O. F. X. Almeida

(see pages 11061–11070)

Amyloid- β (A β) fibrils accumulate into plaques associated with Alzheimer's disease (AD), but soluble A β oligomers may create havoc on their own. This week Roselli et al. investigate a connection between soluble A β oligomers and synaptic proteins. Incubation of cortical cell cultures with freshly dissolved A β_{1-40} peptide (10 μ M; 15–120 min) reduced neuronal expression of the synaptic scaffolding protein postsynaptic density-95 (PSD-95) within 60 min. The authors then used a series of pharmacological and expression assays to examine the signaling pathway involved. The downregulation depended on NMDA receptor activity, calcium influx, and cyclin-dependent kinase 5 (cdk5) activity, and involved the proteasome pathway. Subsequently, surface expression of the AMPA receptor glutamate receptor subtype 2 also declined. A β_{1-40} did not affect expression levels of a PSD-95 mutant that lacked the cdk5 phosphorylation site or ubiquitination motif. These *in vitro* studies suggest one relatively rapid means by which soluble A β oligomers could affect synaptic function.