less efficient precursors. Andrew Shreve (LANL) presented a rich variety of self-assembled nanomaterials that display specific emergent properties of a mechanical, photonic, or fluidic nature.

Computational methods are now powerful enough to suggest new experiments. Yi Jiang (LANL) reviewed the state of the art for molecular multiscale simulations in which the challenge is to connect realistic but slow molecular dynamic simulations with less accurate but fast higher level simulations. Andy Pohorille (NASA Ames Research Center, California) used simulations to argue that nongenomic early organisms could undergo evolution before the origin of organisms with genes. Takashi Ikegami (Univ. of Tokyo) presented simulations of a simple and abstract model of metabolic chemistry that demonstrates the spontaneous formation and reproduction of cell-like structures.

The workshops started with some tension between the origin of life perspective and the more general concern with synthesizing the simplest possible artificial cells. However, the participants eventually agreed that different artificial cell proposals might suggest different prebiotic niches. The workshop ended with a road-mapping exercise on four interrelated issues: (i) What is the boundary between physical and biological phenomena? (ii) What are key hurdles to integrating genes and energetics within a container? (iii) How can theory and simulation better inform artificial cell experiment? (iv) What are the most likely early technological applications of artificial cell research?

In time, research on these forms of artificial life will illuminate the perennial questions "What is life?" and "Where do we come from?" It will also eventually produce dramatic new technologies, such as self-repairing and self-replicating nanomachines. With metabolisms and genetics unlike those of existing organisms, such machines would literally form the basis of a living technology possessing powerful capabilities and raising important social and ethical implications. These issues were elaborated by Bedau, who suggested that the pursuit of these new technologies should be guided by what he called a "cautious courage" perspective. All workshop participants agreed that useful artificial cells will eventually be created, but there was no consensus about when.

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PLANT SCIENCES

A *CONSTANS* Experience Brought to Light

John Klejnot and Chentao Lin

Each year during the spring, nature treats us to an amazing display of color and fragrance. Many plants bloom at this time of the year in response to seasonal changes of day length, a phenomenon called photoperiodism (*1*). Some plants, like Mendel's garden pea or today's experimental favorite *Arabidopsis*, flower more readily as days lengthen in the spring, whereas others such as rice or soybean prefer to flower when days get shorter in the fall. Since the discovery of photoperiodism in plants some 80 years ago (*1*), photoperiodic responses have been widely found in other organisms including mammals (*2*). How plants recognize photoperiods and respond to them by bringing forth blossoms has fascinated biologists for decades. On page 1003 of this issue, Valverde and colleagues (*3*) take us one step closer to understanding this phenomenon.

In plants, light signals are perceived by photoreceptors, which include phytochromes (phy) that respond to red/far-red light and cryptochromes (cry) that respond to blue/ultraviolet-A light (*4*). The light signals are "memorized" by the circadian clock and executed by transcription factors, which activate the floral meristem identity genes that initiate the transition from vegetative growth to reproductive development (*5*). Because neither the photoreceptors nor the circadian clock alone is sufficient to explain photoperiodic flowering, these components must somehow work together to measure day length changes (*5*). Almost a decade ago, Coupland's group discovered that an *Arabidopsis* gene called *CONSTANS* (*CO*) encodes a transcription factor that is critical for photoperiodic flowering (*6*). The CO protein activates the transcription of genes required for floral initiation, including a gene called *FLOWER LOCUS T* (*FT*) (*7*). The transcription of *CO* is governed by the circadian clock in a day length–dependent manner, and it has been hypothesized that a posttranscriptional regulatory mechanism must also be involved in regulating *CO* activity (*7*–*9*). Valverde *et al*. now show that the CO protein is ubiquitinated and then degraded by a protein complex called the proteasome, and that this process is regulated by both phytochromes and cryptochromes.

The researchers used transgenic *Arabidopsis* plants that constitutively express the *35S::CO* transgene independent of transcriptional control by the circadian clock and the *FT::LUC* reporter gene as a readout of *FT* promoter activity. They discovered that despite constitutive *CO* mRNA expression in the transgenic plants, the CO protein level was higher in the light phase of long days than in the light phase of short days, resulting in increased FT promoter activity during long days. Moreover, the abundance of CO protein and the activity of the *FT* promoter were greater in seedlings exposed to white, blue, or far-red light, relative to those exposed to red light or left in the dark. When recombinant CO protein was added to nuclear extracts of plant cells, it became ubiquitinated and degraded; degradation of CO was suppressed by proteasome inhibitors. Thus, CO is degraded in the dark via a ubiquitin/proteasome mechanism, and CO proteolysis is suppressed in light (blue and far-red).

To examine which photoreceptors are responsible for stabilizing CO in response to light, Valverde *et al.* crossed the *35S::CO* transgene into various photoreceptor mutant *Arabidopsis* plants. Analysis of the CO protein in the photoreceptor mutants showed that cry1/cry2 and phyA stabilize the CO protein in blue light and far-red light, respectively, and that phyB promotes CO degradation in red light. Apparently, these photoreceptors act to balance the abundance of CO protein in plants grown under conditions of natural light composed of different wavelengths (see the figure). Because both CO and FT activate flowering, these results also provide an explanation for why the *cry1cry2* and *phyA* mutants flower later than wild-type plants in blue light and far-red light, respectively; why the *phyB* mutant flowers earlier in red light; and how cry2 and phyA antagonize phyB action in white light to control flowering time (*10*, *11*). The

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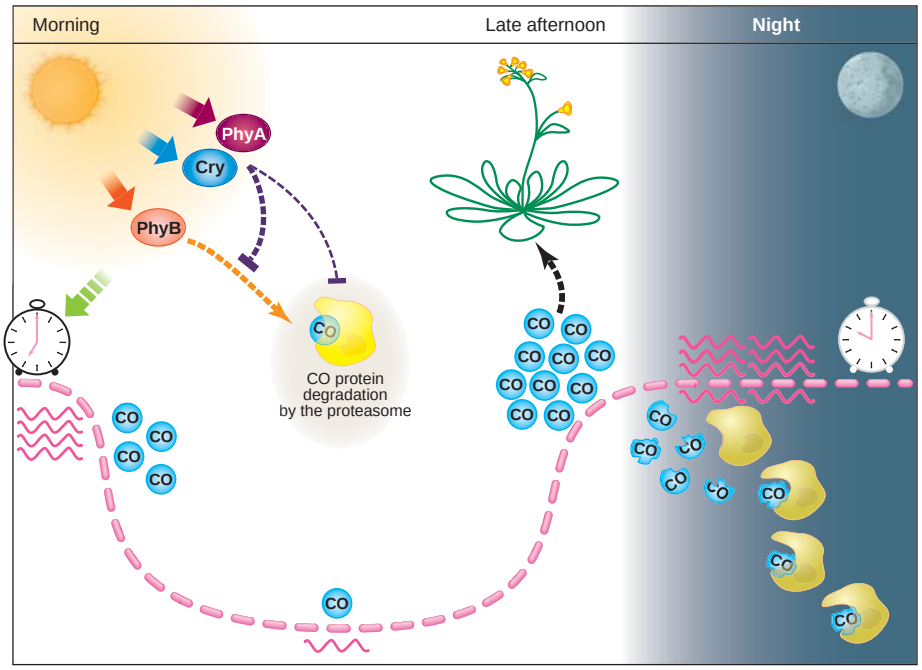

To flower or not to flower. The interplay of photoreceptors and the circadian clock in the regulation of CO expression. *CO* mRNA levels (wavy magenta lines) are regulated by the circadian clock, which is entrained through the action (green arrow) of phytochrome and cryptochrome (Cry) photoreceptors. The peak circadian rhythm of *CO* mRNA expression (dashed magenta curve) runs from the late afternoon to the early morning. CO protein levels (depicted by the number of blue spheres) are determined not only by *CO* mRNA expression, but also by protein degradation in the proteasome (yellow). CO degradation is promoted by phyB, but is inhibited by Cry and phyA during the day. During the night, the amount of CO mRNA remains high, but little CO protein accumulates because of CO proteolysis. During long days, phyA and Cry help to maintain the higher CO protein levels that promote flowering. (Arrows indicate stimulatory actions; lines with bar-head represent inhibitory actions; dashed lines suggest the involvement of additional proteins.)

photoreceptor regulation of CO degradation, coupled with the circadian clock that generates photoperiodic response rhythms of *CO* transcription, enables plants to have a lower amount of CO protein in short days and to gradually increase the level of CO protein as day length increases. Similar mechanisms are probably also at work in rice, a short-day plant, in which CO acts as a transcription suppressor of FT to inhibit flowering during long days (*12*).

It remains puzzling why CO abundance in wild-type plants peaks in the late afternoon or evening of a long day, but not in the early morning when its mRNA level is also relatively high. It is possible that the activity of phyA, cry2, or phyB may oscillate during the light phase of a long day, even though the amount of these photoreceptors remains relatively constant during long days (*11*, *13*). Alternatively, the abundance or activity of other proteins that are involved in CO degradation may be controlled by the circadian clock such that they fluctuate throughout the light phase of a long day. Identification of proteins fingering CO for destruction will help us to solve this puzzle. Some recent studies of *Arabidopsis COP1* and *ZTL* genes, which are involved in light responses or photoperiodic flowering, are noteworthy in this regard. *COP1* encodes a RING-finger protein with WD-40 repeats that is responsible for the proteasome-mediated degradation of the transcription factor HY5 in the dark (*14*); *ZTL* encodes a LOV-domain/F-box protein that is required for the proteasome and circadian clock–dependent degradation of the clock protein TOC1 (*15*). Could COP1, ZTL, or ZTL-related proteins also play a part in the CO degradation reported by Valverde and co-workers? Chances are we may not need to wait until next spring for an answer.

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DEVELOPMENT

Making Sense of the Sensory Lineage

Marianne Bronner-Fraser

Neural crest cells, a uniquely vertebrate cell type, are characterized by their ability to migrate throughout the developing embryo and to form many diverse tissues. These cells arise within the developing central nervous system and subsequently migrate away, sometimes moving extremely long distances to populate peripheral regions of the embryo (see the figure). Neural crest cells are multipotent progenitors that give rise to an impressive array of cell types, including neurons and glia of the peripheral nervous system, cartilage and bones of the face, and melanocytes (pigment cells) (*1*). Perhaps the best studied neural crest derivatives are the peripheral ganglia, which comprise neurons and support cells that form as aggregates outside the brain and spinal cord. These contain neurons of many different flavors, including sensory neurons (which relay touch and pain information to the brain) and autonomic neurons (which innervate various organs and modulate their activity). A report on page 1020 of this issue by Lee *et al.* (*2*) sheds light on the mechanism through which sensory neurons are generated from multipotent neural crest progenitor cells.

The fact that neural crest cells give rise to so many different progeny has raised the fascinating question of whether they are "stem cells." A stem cell divides to form one multipotent daughter cell like itself and another that is biased toward a particular cell fate. In support of the idea that neu-

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