Bidirectional transcription of *Tetrahymena* IESs during meiosis [12] generates double-stranded RNAs that are cleaved by a Dicer-like ribonuclease [13,14] into ~28 nucleotide short RNAs, called scan RNAs [15]. These short RNAs are transported into the developing somatic macronuclei where they target the methylation of lysine 9 of histone H3 on chromatin associated with the homologous sequence, which then signals DNA elimination [14,16,17]. Several lines of evidence have suggested that scan RNAs are first transported into the maternal macronucleus, where any encounter with the homologous DNA sequence, or possibly with a RNA transcript, results in the removal of that short RNA from the pool that will direct chromatin modification in the developing macronucleus [15,18].

If, in *Paramecium*, the comparison between genomes occurs in the maternal macronucleus, any protective maternal transcripts should act before the relocalization of the Nowa proteins. Then the Nowa proteins could very well be involved in transporting to developing macronuclei the positively acting RNAs that direct DNA elimination. Loss of such a protein would inhibit DNA rearrangement as observed.

Is such sequence-specific comparison of maternal and developing genomes limited to ciliates that conveniently carry both in a common cytoplasm? This need not be the case. RNAi-related mechanisms utilized by these organisms to direct DNA rearrangements are commonly used throughout eukaryotes to silence specific regions of the genome [19]. Many biological phenomena await explanations: for example, the specific reversion of the *hothead* mutation in *Arabidopsis* even several generations removed from copies of the wild-type allele is one of the more recently described enigmas [20]. Could it be that a maternal copy of the genome can be kept in reserve and used to alter development? This is pure speculation, but the characterization of the Nowa proteins again shows that mom has her ways to impose her influence.

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Photosensing Fungi: Phytochrome in the Spotlight

Red light triggers asexual development and represses sexual development in the fungus *Aspergillus nidulans*. This response has been shown to require a phytochrome red/far-red light photoreceptor, FphA, which is cytoplasmic and binds a tetrapyrrole chromophore. FphA exhibits similarities to both plant and bacterial phytochromes.

Alexander Idnurm and Joseph Heitman

Organisms sense light to regulate growth, control development or capture energy for photosynthesis. Members of the fungal kingdom, which are heterotrophs, can respond to wavelengths of light from UV-C to far-red; however, until recently only one photoreceptor class of blue light sensors had been identified in fungi. The report in this issue of *Current Biology* by Blumenstein *et al*. [1] on red light sensing via a phytochrome in the model fungus *Aspergillus nidulans* is a milestone in photobiology. In addition to identifying a second

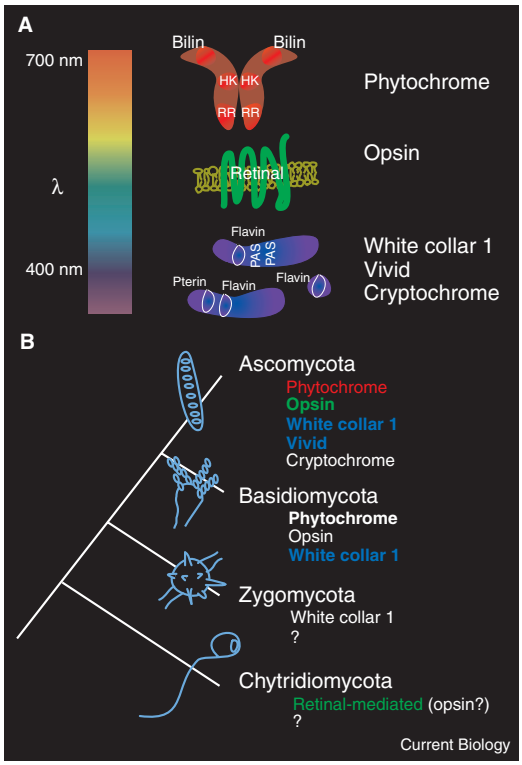

Figure 1. Photons are sensed in the fungal kingdom by proteins conserved in other kingdoms.

The FphA phytochrome of *A. nidulans* represents a new photoreceptor governing red/far-red photoperception. (A) Fungi respond to wavelengths (λ) across the visible spectrum: red/far-red is sensed by phytochrome (HK, histidine kinase; RR, response regulator) [1], green by opsin and blue/UV-A by white collar 1 (PAS, Per-Arnt-Sim) and VIVID, and possibly cryptochromes. The chromophores with which these proteins interact are indicated. (B) There is evidence based on photoresponse and gene homology for conserved photoreceptors throughout the fungal kingdom. Those colored have been shown to function in response to light (WC-1 in the ascomycetes *Neurospora crassa* and *Trichoderma atroviride* and the basidiomycetes *Cryptococcus neoformans* and *Coprinus cinereus*; VIVID in *N. crassa*; opsin in *N. crassa* and *Leptosphaeria maculans*). With partial genome coverage, the possibility of novel photoreceptors, and unresolved relationships at the base of the kingdom, the fungi have much yet to reveal about how they sense light.

photoreceptor-type in the fungi, it extends the importance of phytochromes in regulating development and other responses to red light from the plant and bacterial kingdoms into the fungal kingdom.

While photoreceptors mediate complex developmental and other responses, they rely on relatively simple structures. All sport a domain that physically interacts with a small, light-sensitive molecule, the chromophore, and have a way of communicating the impact of a photon to the rest of the cell or organism (for a recent review, see [2]). Photoreceptors in animals include the opsins, which contain seven transmembrane helices and bind the chromophore retinal, and cryptochromes, which bind flavins and pterins and are related to the photolyase family but do not function in DNA repair. The plant kingdom contains an enormous array of photoreceptors, probably reflecting their ubiquitious interactions with light, including cryptochromes, and phototropins which also bind flavin and function in phototropic responses. The plant phytochromes bind a tetrapyrrole molecule and sense red and far-red light to control the circadian clock, together with cryptochromes. Phytochromes exist in two photo-interconvertible states: an inactive Pr form and an active Pfr form. Red light shifts the conformation to the Pfr form, and far-red shifts it to the Pr form, while in the dark there is gradual reversal of the Pfr form to the Pr form. Slime mold and bacteria also contain phytochromes (the latter additionally contain other classes of photoreceptors, such as xanthopsins).

Fungi are ideal for investigating photobiology. They are often haploid, so a single mutation results in a phenotype; they can sense light wavelengths across the visible spectrum and over a large dynamic range, from star light to full sun light; and physiological evidence and genome sequencing projects have revealed that the four classes of photoreceptors found in other kingdoms are conserved in the fungi (Figure 1). For example, the model photosensor *Neurospora crassa* encodes the blue light receptors WC-1 and VIVID, which contain a flavin binding LOV (light, oxygen, voltage) domain like those of the plant phototropins and other plant photoreceptors [3–5]. Replacing the WC-1 LOV domain with that of the plant photoreceptor Phot1 or FKF1 yields a protein that is hyperphosphorylated in response to light [6]. *N. crassa* also contains a green-light absorbing opsin that binds retinal [7], a cryptochrome and two phytochromes. These *N. crassa* photoreceptors are all of as yet unknown physiological function [8].

In fungi other than *N. crassa*, far less is known about mechanisms of photosensing although photobiological responses have been reported from over a hundred species. The existence of an opsin that functions in phototaxis is supported by studies in a basal fungus, the chytrid *Allomyces reticulatus* [9], and a green-responsive opsin from *Leptosphaeria maculans* can pump protons [10]. The WC-1/WC-2 blue light sensing system was recently documented to function in the basidiomycete phylum of fungi that diverged from *N. crassa* more than 500 million years ago [11]. A phytochrome-like red/far-red light sensor has been suggested in ascomycetes and basidiomycetes for decades [12–14], yet no protein has been characterized.

Aspergillus nidulans now steps into the limelight within this context of extensive evidence for photosensing and the growing genomic evidence for photoreceptors. Red light is the 'stop' signal for sexual development and a 'go' signal for asexual development in this fungus. *A. nidulans* senses red and far-red light in a manner reminiscent of the plant phytochromes; red light enhances the production of asexual spores (conidia) and a far-red pulse blocks this induction [15]. In darkness, the sexual pathway is enhanced. This inconvenience for researchers, who want robust

conidiation, has meant that for 50 years the standard 'wild-type' laboratory strains bear a mutation in the gene *velvet* (*veA*) that causes spontaneous conidiation in both the light and dark; *velvet*'s function in mediating asexual–sexual development remains elusive.

The regulation of conidiation is of major importance for fungi – a conidiating culture can produce millions of aerially dispersed spores. For the laboratory model *A. nidulans*, this occasionally leads to laboratory contamination, but if spores from its close relative *A. fumigatus* enter the lungs of an immunocompromised patient they may establish a life-threatening infection. The *Aspergillus* genus also contains species that infest corn and other plants and produce carcinogenic molecules like aflatoxins, while others are used in food processing and biotechnology. Sexual reproduction is vital in many fungi for dispersal and for creating genetic diversity that can maintain fit populations in diverse environments. Thus, understanding how *Aspergillus* and other fungi sense their environment is of intellectual, medical and industrial importance.

Blumenstein *et al*. [1] have demonstrated that the *A. nidulans* FphA protein expressed in *Escherichia coli* binds biliverdin and absorbs red and far-red light. Mutation of a cysteine residue conserved in the bilin binding domain of other phytochromes resulted in a protein no longer able to absorb these wavelengths. Deletion of the *fphA* gene, which is present in a single copy, renders *A. nidulans* partially insensitive for red light suppression of sexual development. Curiously, in a *fphA* mutant strain the proportion of sexual fruiting structures (cleistothecia) is not as high in red light as in darkness, and thus the authors suggest the presence of a second red light-sensing system.

Blumenstein *et al*. [1] found that a fusion between FphA and green fluorescent proteins localizes to the cytoplasm and is excluded from nuclei, suggesting that red-light photoperception may occur in the cytoplasm. This is in contrast to the functions of plant phytochromes which are cytoplasmic in darkness, and then a fraction localized to the nucleus in response to light [16]. Like plant photoreceptors, however, FphA functions as a multimeric complex. These exciting discoveries clearly show phytochrome functioning in red/far-red signaling in the fungi, likely important for sensing dawn and dusk to adjust for circadian variations.

At a structural level, Blumenstein *et al*. [1] note that fungal phytochromes are more similar to bacterial than plant phytochromes, because they contain a phytochrome region and histidine kinase domain combined in a single protein, with an additional carboxy-terminal response regulator domain. Intriguingly, at a regulatory level, *A. nidulans* red-light sensing also resembles plants via the involvement of protein degradation pathways. *A. nidulans* mutants defined in light-sensing have been previously isolated and some lack components of the COP9 signalosome (named for *Arabidopsis* `constitutively photomorphogenic' mutants); a *csnD* mutant shows constitutive sexual development in the light [17]. The COP complex mediates red light signaling by phytochromes in *Arabidopsis*, with COP1 acting as an E3 ubiquitin-ligase to regulate 26S proteosome degradation of PhyA and the downstream PhyA targets HY5 and LAF1, both transcription factors [18]. Thus, the FphA protein is structurally similar to the bacterial phytochromes, and yet the red light signal is regulated via a similar mechanism to that used in plants.

For others pursuing fungal photoreceptors, the research by Blumenstein *et al*. [1] raises two important points. First, that strain background can have a major impact on light-sensing, reminiscent of what is known about differences in phytochrome signaling in accessions of plants [19]. The phenotype of FphA is masked by the *veA* mutation in the *A. nidulans* laboratory strains. In contrast, many photobiology experiments of *N. crassa* work best in a *band* (*bd*) mutant background. While *A. nidulans* development is predominantly a red-light-mediated response, a mutant strain *bliA1* has been characterized that now also senses blue light, with the opposite effects of red light [20]. The second issue is that the chromophore may not be available to the fungus *in vitro* and may need to be supplemented. Blumenstein *et al*. [1] see no evidence for a heme oxygenase in the *A. nidulans* genome that could provide the bilin chromophore for FphA.

Future research in *A. nidulans* will be to characterize the target proteins of FphA. Are these cytoplasmic and directly affecting development, or does FphA act on a protein that is then targeted to the nucleus? The VeA protein, which enhances sexual reproduction and represses asexual reproduction, represents an obvious downstream FphA candidate. The last 12 months have seen reports on photoreceptors in diverse fungi; this research [1] shows that *A. nidulans* represents an excellent system for illuminating how photons regulate plant, bacterial and fungal biology.

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Neuroscience: Comraderie and Nostalgia in Nematodes

Two recent papers on social rearing and olfactory imprinting show that early developmental experiences can lead to long-lasting changes in behaviour of the model nematode *Caenorhabditis elegans*.

Cori Bargmann

To what extent is the nervous system organized by genetic templates, and to what extent is it reorganized by experience? Since Hubel and Wiesel [1] showed that closing one eye leads to rewiring of eye-specific columns in the visual cortex, physiologists and anatomists have explored the relationship between sensory activity and wiring. A similar question about early experience has been asked by ethologists since Lorenz [2] in their studies of imprinting, a process in which sensory experiences early in development lead to long-lasting changes in an animal's behavior. The most familiar example of imprinting may be the olfactory imprint that allows adult salmon to return to the river in which they were spawned.

The soil nematode *Caenorhabditis elegans* is known for a dramatic response to early developmental experience. At the end of its first larval stage, each animal integrates three sensory inputs — a pheromone, chemical cues from food, and temperature—to decide whether to become a feeding third-stage larva or a developmentally arrested dauer larva, which has a distinct morphology, physiology, and behavior [3]. The dauer decision can be viewed as an extreme form of experience-dependent plasticity, and it shows clearly that the sensory nervous system has powerful access to the nematode's biology. But to what extent is the dauer decision a special case? Does the simple nematode nervous system, composed of just 302 neurons, have the flexibility to remodel itself in response to other sensory information?

Rankin and colleagues [4] addressed this question using a biologically relevant source of sensory information: the presence of conspecific individuals. They compared animals raised in isolation on a bacterial lawn to animals raised in colonies of 30 to 40 animals. At this density, dauer larvae do not form, food is in vast excess, and the small nematodes spend most of their time alone, occasionally encountering another individual.

There are strains of *C. elegans* that aggregate on lawns, but the strain used in this experiment is solitary, and the animals appear to pay little attention to each other. But appearances can be deceiving. In fact, the animals raised in small colonies were strikingly different from isolate-reared animals as adults. Group-reared animals had a much stronger avoidance response to mechanical stimuli than animals raised in isolation. Colony growth also accelerated the rate of development, so that animals grew larger and reached the adult stage about 4 hours earlier (at ~70 hours of development) than isolated animals.

An increase in mechanical stimulation in colonies, presumably because of collisions between animals, may explain the stronger avoidance behavior of group-reared animals. A brief, intense mechanical stimulation increased the avoidance responses of isolated animals almost to the level seen after group rearing, but did not change the behavior of group-reared animals. The AMPA-type glutamate receptor GLR-1, which has a relatively minor role in mechanosensation per se, is required for this effect. GLR-1 is prominently expressed on, and affects the activity of, the giant