# Fungi, Hidden in Soil or Up in the Air: Light Makes a Difference

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## Key Words

light sensing, phytochrome, signal transduction, *Aspergillus*, secondary metabolism, development

## Abstract

Light is one of the most important environmental factors for orientation of almost all organisms on Earth. Whereas light sensing is of crucial importance in plants to optimize light-dependent energy conservation, in nonphotosynthetic organisms, the synchronization of biological clocks to the length of a day is an important function. Filamentous fungi may use the light signal as an indicator for the exposure of hyphae to air and adapt their physiology to this situation or induce morphogenetic pathways. Although a yes/no decision appears to be sufficient for the light-sensing function in fungi, most species apply a number of different, wavelength-specific receptors. The core of all receptor types is a chromophore, a low-molecular-weight organic molecule, such as flavin, retinal, or linear tetrapyrrols for blue-, green-, or red-light sensing, respectively. Whereas the blue-light response in fungi is one of the best-studied light responses, all other light-sensing mechanisms are less well studied or largely unknown. The discovery of phytochrome in bacteria and fungi in recent years not only advanced the scientific field significantly, but also had great impact on our view of the evolution of phytochrome-like photoreceptors.

## Contents



**Phytochrome:** red- and far-red-sensing chromoprotein, with a linear tetrapyrrol as chromophore; switches between two states depending on the light conditions

## INTRODUCTION

The light environment on Earth varies strongly throughout the day in both quality and intensity. Plants, which cannot actively choose their surroundings, need to modify their growth and development to optimize their utilization of ambient light. As early as 1880, Charles Darwin had noted, "No one can look at the plants growing on a bank or on the borders of a thick wood, and doubt that the young stems and leaves place themselves so that the leaves may be well illuminated" (29). One important light sensor in plants is phytochrome.

Phytochrome has been described as a light-sensor protein, associated with a linear tetrapyrrol undergoing *cis-trans* isomerization after red-light absorption. The conformational changes of the chromophore are transmitted within the protein and initiate a signal-transduction cascade ultimately resulting in differential gene expression. One important phenomenon described in Darwin's *Origin of Species* is the shade-avoidance reaction (72). Plants are normally competing for sunlight; thus, it was evolutionarily advantageous for plants to develop systems to measure the light conditions and adapt their growth behavior. In this respect, the shade-avoidance reaction can be seen as one of Darwin's postulates of the "struggle for existence." Indeed, the ratio between red and far-red light can be a much better measure for the density of plants than the intensity of an individual wavelength. Normal daylight consists of an almost-balanced ratio between red and far-red light. However, light in a plant environment is far-red shifted, because of red-light absorption, scattering, and reflection of the leaves.

Intense research on the red-light response in plants was initiated in the 1950s when phytochrome was analyzed and the first enrichment procedures for the pigment-containing protein were established (22). Approximately 40 years later, the first phytochrome was discovered outside the plant kingdom in the cyanobacteria *Synechocystis PCC6803* and *Fremyella diplosiphon* (63, 66, 75). However, even more surprising was the discovery of phytochrome-like sequences in the heterotrophic bacteria *Deinococcus radiodurans* and *Pseudomonas aeruginosa* (12, 30) and in the fungal kingdom (15). These discoveries suggest that phytochrome must have evolved millions of years before the emergence of green plants. In addition to phytochrome, plants employ a blue-light-sensing system and animals use opsins for photosensing (27, 36).

Fungi, however, appear to employ both plant and animal photosensors. This review summarizes some recent molecular aspects of light sensing in fungi with special emphasis on phytochrome signaling.

## LIGHT SENSING IN FUNGI

Fungi are eukaryotic microbes that sense and interact with the surrounding environment (4). Most fungi are saprophytic organisms and their growth depends on the availability of organic matter. Thus, they live in soil or in the organic matter. However, they may coincidentally reach the surface and then their habitat may change drastically. When the humidity is stable in soil, the mycelium may desiccate quickly when exposed to the surface. One major change is also the exposition to light and thus to dangerous ultraviolet irradiation. This may cause DNA damage and a dramatic increase of harmful reactive oxygen species.

Fungi are potent producers of secondary metabolites, such as antibiotics or mycotoxins (17, 132), which are most likely produced for chemical warfare. The need to generate such a mix of chemicals may also be different if the fungus grows in soil or on a surface. Light can serve as a fast indicator of the expected changes and thus is a useful trigger for adaptation to this harsh environment outside the substrate (**Figures 1** and **2**).

Another important phenomenon concerns reproduction. For sessile saprophytic fungi, it is crucial to escape the substrate to produce spores so the fungi can spread in the environment (42). Many of the described changes occur not only when fungi leave their substrate, but also during the night-day cycle. Because adapting the physiology preferred during the day before the sun rises is advantageous, it is not surprising that many fungi have a circadian clock. As in higher organisms, this clock is light and temperature compensated (21, 32, 87).

Another fascinating aspect is not only the sensing of light intensity, but also, in some species, of the direction of illumination, leading to phototropic responses (110). This response

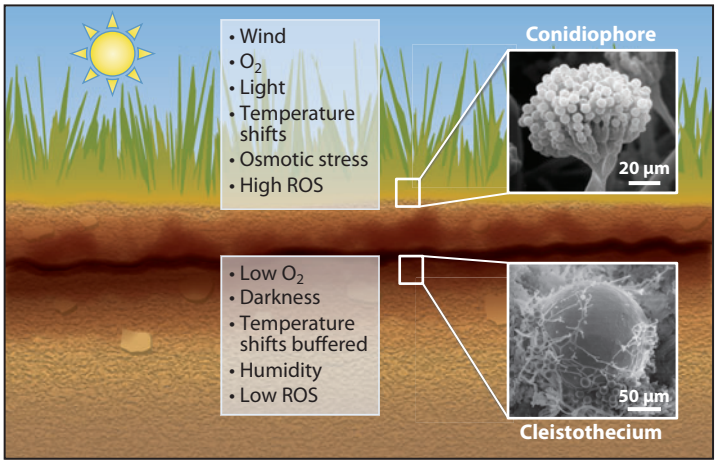



**Figure 1**

Summary of the conditions in soil and at the surface. The pictures show a conidiophore of *Aspergillus nidulans*, which is produced on the surface, and a cleistothecium produced in the substrate. ROS, reactive oxygen species.

is important for the optimization of spore dispersal. A summary of light responses in different fungi is given in **Figure 2**.

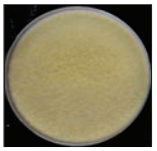
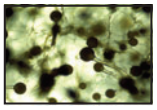
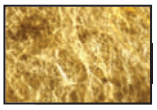
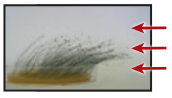
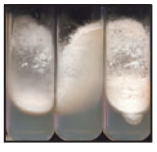
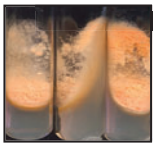
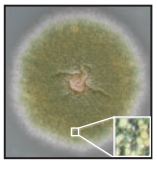
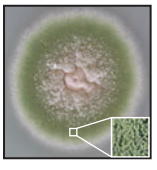
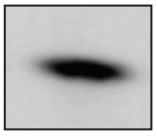
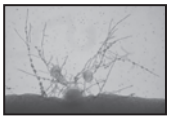
Despite the large number of light-dependent processes in fungi and the amenability of many fungi to molecular biological, biochemical, and cell biological methods, the knowledge about the exact mechanisms of light perception and signal transduction is limited. Only the blue-light response has been studied intensively, especially in *Neurospora crassa*. However, the discovery of phytochrome some years ago stimulated several laboratories to investigate the molecular biology underlying different light responses. The increasing number of fungal genome sequences revealed the presence of a number of different photoreceptors in each fungus and suggests fascinating but rather complex and diverse regulatory systems (**Figures 3** and **4**).

## THE WHITE-COLLAR SYSTEM: THE FIRST AND BEST-STUDIED PHOTORECEPTOR SYSTEM IN FUNGI

Blue-light responses in *N. crassa* include the induction of sporulation and protoperithecia

**Chromophore:** low-molecular-weight cofactor that enables a protein to absorb light of specific wavelengths

**Circadian clock:** intrinsic feedback loop that allows organisms, independent of external factors, to orientate themselves to daytime

| Phylum | Organism | Dark | Light |
|---|---|---|---|
| Zygomycota | *Phycomyces blakesleeanus* | | |
| | **Photocarotenogenesis**<br>Induction of carotenoid biosynthesis in mycelium |  |  |
| | **Photomorphogenesis**<br>Inhibition of microphore formation |  |  |
| | **Phototropism**<br>Orientation of macrophores toward light |  |  |
| Ascomycota | *Neurospora crassa* | | |
| | **Photocarotenogenesis**<br>Induction of carotenoid biosynthesis |  |  |
| | **Circadian clock control**<br>Set the time of the circadian clock |  | |
| | *Aspergillus nidulans* | | |
| | **Photomorphogenesis**<br>Inhibition of sexual development and induction of asexual development |  |  |
| | **Secondary metabolism control**<br>Inhibition of sterigmatocystin synthesis |  |  |
| Basidiomycota | *Coprinopsis cinerea* | | |
| | **Photomorphogenesis**<br>Fruiting body maturation |  |  |
| | *Cryptococcus neoformans* | | |
| | **Photomorphogenesis**<br>Inhibition of mating and haploid fruiting |  |  |

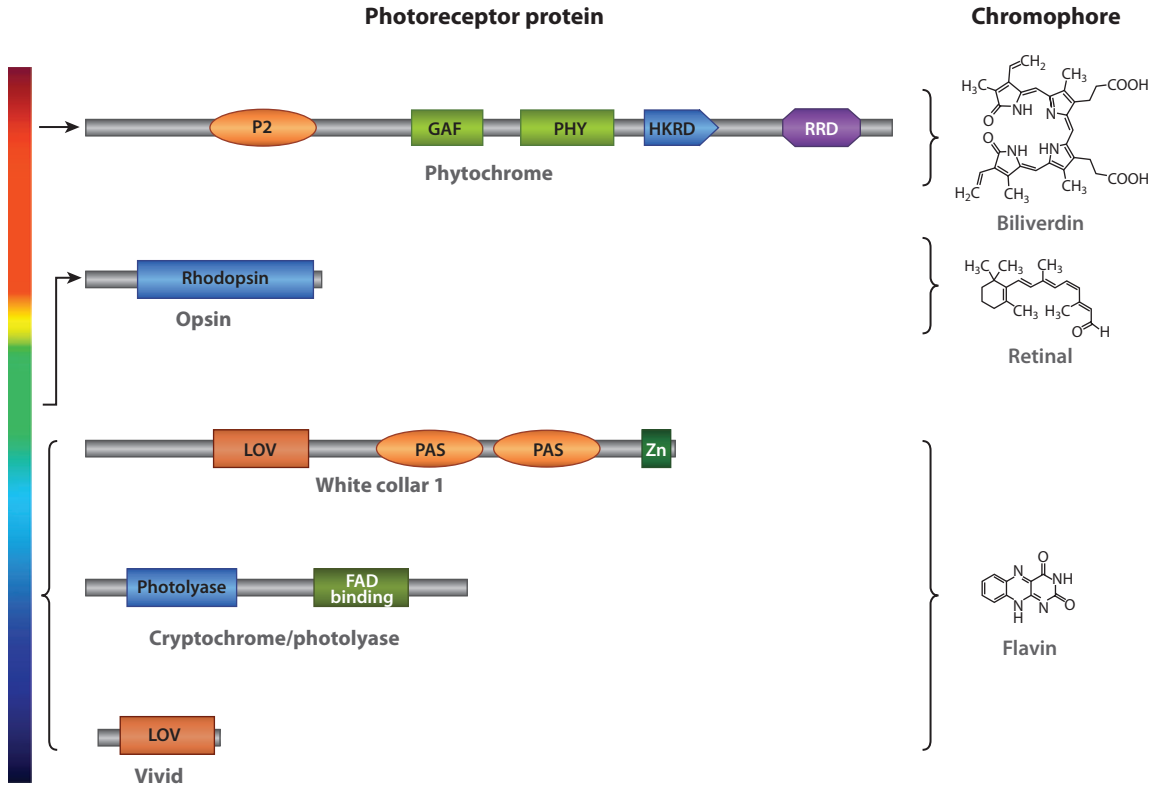



**Figure 3**

Scheme of the general architecture of fungal light receptors and their chromophores (shown as chemical structures). Proteins sizes range from 1280 amino acids for the *Aspergillus nidulans* FphA protein to 186 amino acids for the *Neurospora crassa* Vivid protein. See text for an explanation of the domain nomenclature. Cryptochrome/photolyase proteins contain pterin molecules as an additional chromophore.

development (60), positive phototropism of perithecial beaks (49), the induction of the synthesis of carotenoids (50), and the regulation of the circadian clock (111). All the different responses require the *wc-1* and *wc-2* genes (5, 81). They were identified in a genetic screen for strains with defects in the carotenoid biosynthesis. *N. crassa* produces carotenoids in

**Figure 2**

Overview of photoresponses in different fungi. In *Phycomyces blakesleeanus*, light stimulates carotenoid biosynthesis but inhibits microphore formation. One striking response is the phototropic response of macrophores. The arrows indicate the direction of illumination (right-hand-side picture was taken from Reference 58). In *Neurospora crassa*, carotenoids color the mycelium (here grown in test tubes) orange. On an agar plate, *N. crassa* forms concentric rings indicating rhythmic sporulation. This rhythmicity continues in the dark illustrating the presence of a circadian clock. The circadian clock is light compensated (picture provided by Christian Heintzen). In *Aspergillus nidulans*, the balance between asexual and sexual development is light dependent. In the dark, more sexual fruiting bodies (*yellow structures in the inset*) are produced, whereas in the light, green-colored asexual conidiospores are dominating. Sterigmatocystin (ST) biosynthesis (a precursor of aflatoxin) is enhanced in the dark. The picture shows an ST band after thin-layer chromatography. In *Coprinopsis cinerea*, fruiting-body development depends on blue light (picture provided by W. Chaisaena; Reference 71). In *Cryptococcus neoformans*, fruiting filament and blastospore production are light dependent. The picture shows the border of a yeast colony incubated for 7 days in dark or light (picture taken from Reference 57). The phylogenetic classification of basal fungal lineages is still under discussion. We therefore keep the traditional name Zygomycota (55, 128).

| | PHY | WC-1 WC-2 | OPS | CRY | VVD | VEL | FRQ | HO |
|---|---|---|---|---|---|---|---|---|
| **Basidiomycota** **Agaricomycotina** | | | | | | | | |
| *Coprinopsis cinerea* | 1 | 1/1 | None | 1 | None | 1 | None | 1 |
| *Laccaria bicolor* | None | 1/1 | None | None | None | 1 | None | 1 |
| *Pleurotus ostreatus* | 1 | 1/1 | None | 1 | None | 2 | None | 1 |
| *Cryptococcus neoformans* | 1 | 1/1 | 1 | None | None | 1 | None | 1 |
| **Ustilaginomycotina** | | | | | | | | |
| *Ustilago maydis* | 1 | 1/1 | 3 | 4 | None | 2 | None | 1 |
| **Ascomycota** **Euascomycota (Pezizomycotina)** **Eurotiomycetes** | | | | | | | | |
| *Aspergillus nidulans* | 1 | 1/1 | 1 | 1 | None | 1 | None | None |
| *Aspergillus terreus* | 1 | 1/1 | 2 | 1 | None | 1 | None | None |
| *Aspergillus niger* | 1 | 1/1 | 2 | 2 | None | 1 | None | None |
| *Aspergillus fumigatus* | 2 | 1/1 | 1 | 1 | None | 1 | None | None |
| *Aspergillus oryzae* | 1 | 1/1 | 1 | 1 | None | 1 | None | None |
| *Aspergillus flavus* | 1 | 1/1 | 1 | 1 | None | 1 | None | None |
| *Penicillium marneffei* ATCC 18224 | 1 | 1/1 | 2 | 1 | None | 1 | None | 1 |
| *Penicillium chrysogenum* Wisconsin | 2 | 1/1 | 1 | 1 | None | 1 | None | None |
| *Talaromyces stipitatus* | 1 | 1/1 | 2 | 1 | 1? | 1 | 1 | 1 |
| **Sordariomycetes** | | | | | | | | |
| *Fusarium oxysporum* | 1 | 1/1 | 4 | 2 | 1 | 1 | 4 | 1 |
| *Trichoderma reesei* | 1 | 1/1 | None | 2 | 1 | 1 | 1 | 1 |
| *Trichoderma atroviride* | 1 | 1/1 | 1 | 2 | 1 | 1 | 1 | 1 |
| *Neurospora crassa* OR74A | 2 | 1/1 | 2 | 2 | 1 | 1 | 1 | 1 |
| *Chaetomium globosum* | None | 1/1 | 1 | None | None | 1 | None | None |
| *Cryphonectria parasitica* | 1 | 1/1 | 2 | 2 | 1 | 2 | 1 | 1 |
| *Magnaporthe grisea* | 1 | 1/1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **Leotiomycetes** | | | | | | | | |
| *Botrytis cinerea* B05.10 | 2 | 1/1 | 2 | 1 | 1 | 1 | 1 | 1 |
| **Dothideomycetes** | | | | | | | | |
| *Alternaria brassicicola* | 1 | 1/1 | 3 | 1 | 1? | 1 | 1 | 1 |
| **Hemiascomycota** **(Saccharomycotina)** | | | | | | | | |
| *Yarrowia lipolytica* CLIB122 | None | 1/1 | None | None* | None | 1 | None | 1 |
| *Candida albicans* | None | None | None | None* | None | None | None | 1 |
| *Pichia stipitis* | None | None | None | None* | None | None | None | 1 |
| *Saccharomyces cerevisiae* S288C | None | None | None | None* | None | None | None | 1 |
| **Archiascomycota** **(Taphrinomycotina)** | | | | | | | | |
| *Schizosaccharomyces japonicus* | None | 1/1 | None | None* | None | None | None | None |
| *Schizosaccharomyces pombe* | None | None | None | None* | None | None | None | None |
| **Zygomycota** **Mucormycotina** | | | | | | | | |
| *Mucor circinelloides* | None | 3/4 | None | 1 | None | Multiple | None | 2 |
| *Phycomyces blakesleeanus* | None | 3/4 | None | 1 | None | Multiple | None | 1 |

hyphae and conidiophores, giving them an orange appearance (95, 99). However, whereas carotenoid biosynthesis is constitutive in conidiophores, it is light regulated in hyphae. Because colonies of "blind" mutants appeared to have a white collar of unpigmented hyphae, the corresponding 28 mutants were designated *wc*, accordingly. Subsequent studies revealed that only two genes were identified in the mutagenesis approach, *wc-1* and *wc-2* (31).

WC-1 and WC-2 contain zinc-finger motifs for DNA binding and PAS domains for protein-protein interactions. WC-1 and WC-2 interact and form the White Collar complex (WCC). This complex, upon light exposure, binds transiently to the promoters of light-inducible genes, presumably to activate their transcription (43, 53). One of the most interesting open questions concerned the mechanism of light perception and subsequent signal transduction. This question was solved simultaneously in two laboratories. Most surprisingly, the transcription factor WC-1 harbors a flavin (FAD) as a light-sensing chromophore (43, 52). This is bound by a specialized PAS domain called LOV (light, oxygen, and voltage) (5, 6, 28) (**Figure 3**).

Analysis of the circadian clock in *N. crassa* in particular has significantly broadened our overall knowledge about circadian clocks and the functioning of the WCC. The core of the *N. crassa* circadian clock is a negative feedback loop with the WCC as a positive element and the Frequency protein, Frq, as a negative regulator. For details, the reader is referred to some excellent overview articles (20, 32, 87).

In addition to WC-1, proteins VIVID (VVD) and ENVOY (ENV) represent other blue-light photoreceptors in *N. crassa* and *Trichoderma reesei* (*Hypocrea jecorina*), respectively (**Figure 4**). In *vvd* mutants, the induction of light responses is largely normal, but they display some defects in photoadaptation, i.e., the ability of organisms to sense incremental changes in light intensity (116, 119). ENVOY displays high similarity to VIVID but is unable to replace it (113). The *Trichoderma* protein is involved in the conditional adaptation to light, because lack of functional ENVOY does not result in blindness but leads to altered gene expression of light-regulated genes (114). *vvd* and *env1* are both involved in the regulation of light-dependent processes but may also respond to different physiological stimuli.

The WC-light-sensing system has been studied in a number of fungi, such as the ascomycete *Trichoderma atroviride* (24, 47), the phytopathogenic *Magnaporthe grisea* (now called *M. oryzae*) (77) and *Bipolaris oryza* (67), and the basidiomycete *Cryptococcus neoformans*. The functions of the WCC appear to be conserved, and in *C. neoformans*, a role in pathogenicity has been discussed (57). Additional complexity of fungal light-sensing systems was suggested after the identification of several copies of *wc* genes in the zygomycetes *Phycomyces blakesleeanus*, *Mucor circinelloides*, and *Rhizopus oryzae* (three WC-1, four or five WC-2) (84, 110, 120) (**Figure 4**). Given that WC-1 and WC-2 proteins can interact to form a protein complex, many putative protein combinations can be envisaged in zygomycetes.

*Aspergillus nidulans* provides another example of the discovery of additional aspects of light sensing. The decision of vegetative hyphae to undergo either the asexual or the sexual developmental pathway largely depends on light (**Figures 2** and **5*a***). Under light conditions,

**PAS:** period clock (PER) protein, aromatic hydrocarbon receptor nuclear translocator (ARNT), and *Drosophila* single minded (SIM)

**White Collar complex (WCC):** comprises the WC-1 and WC-2 proteins

**Figure 4**

Analysis of 31 fungal genomes for the presence of different photoreceptors and related proteins. Genomes were searched with the Blastp program using standard parameters and the following sequences as queries: *Aspergillus nidulans* ANID_09008 (FphA) only the GAF-PHY domain was used, ANID_03436 (LreA), ANID_03607 (LreB), ANID_01052(VELVET) and *Neurospora crassa* NCU00582 (Cry-1), NCU10055 (NOP-1), NCU03967 (VVD), and NCU02265.3 (FRQ). Proteins identified in this way were analyzed further for characteristic features of the corresponding proteins to confirm their relatedness. However, proteins in most genomes have been annotated automatically and thus the exon-intron structure may be different in some cases. For heme oxygenase (HO), we used the SCOP classification (database based in structural classification of proteins) because protein sequences are poorly conserved.

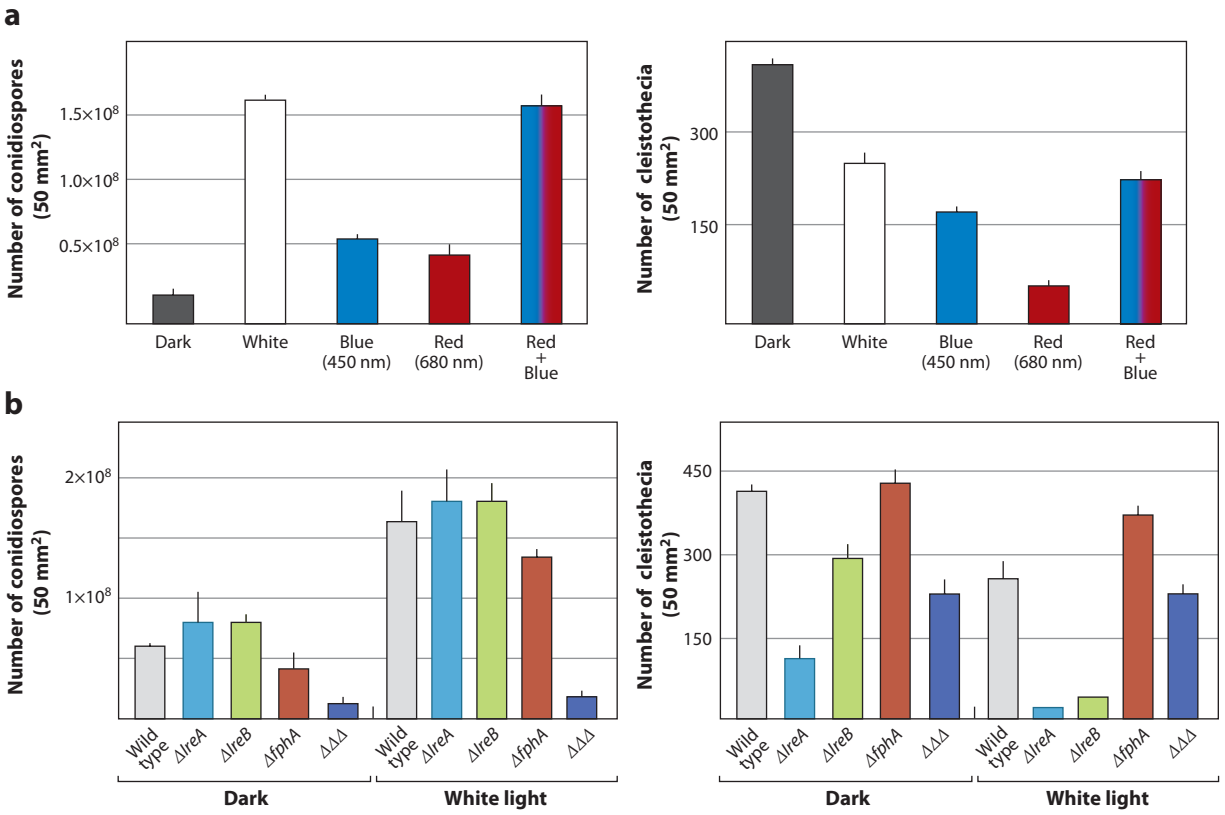



**Figure 5**

Quantification of conidiospores and cleistothecia formation in *Aspergillus nidulans*. (*a*) Comparison between different light conditions: darkness, white, blue (450 nm), red (680 nm), and blue plus red light. (*b*) Effect of the deletion of *fphA*, *lreA*, and *lreB* on conidiospore and cleistothecia formation. Conidiospores and cleistothecia were counted in a 50 $mm^2$ area as described in Reference 101. The graphs show the average of three independent experiments. Error bars represent the standard deviation. ΔΔΔ refers to the triple mutant of Δ*fphA*, Δ*lreA*, and Δ*lreB*.

mainly asexual conidiospores are produced; in the dark, the fungus produces more resistant and durable ascospores. Thus, the light response reflects a balance between the two morphogenetic pathways rather than a yes/no decision. Recently, it was shown that *A. nidulans* senses not only red (see below), as originally described, but also blue light (90, 101). Blue light alone induces the asexual cycle, but it is less effective than white light (or a combination of blue and red light) and it partially inhibits the sexual cycle (**Figure 5*a***). In comparison, blue light represses mycotoxin formation (sterigmatocystin) to the same extent that white light does (**Figure 2**). The corresponding WC orthologs were termed LreA and LreB. Asexual conidiospore production was slightly increased in Δ*lreA* and Δ*lreB* strains, independent of the presence or absence of light. These data suggest a repressing function of LreA and LreB for the asexual cycle. However, they also act as positive factors for the sexual cycle. Most interestingly, LreB interacted not only with LreA, but also with the phytochrome FphA (see below), which also interacted with another regulatory protein, VeA. The latter regulator has been implicated in the red-light response in *A. nidulans* for many years (23, 90), but cloning of the gene revealed that VeA is not a photosensor. Because of the interaction of the blue- and the red-light-sensing

proteins, a WC phytochrome light-regulator complex has been proposed (101). Recent studies showed that VeA may serve additional functions in hyphae (69). VeA physically interacts with a well-known regulator of secondary metabolism, LaeA (9). In addition, it interacts with a Velvet-like protein (VelB) and three other velvet-interacting proteins (VipA,VipB, and VipC) (9, 23), suggesting two different VeA-containing protein complexes. It remains to be determined, however, whether all protein interactions occur at the same time and/or in the same subcellular compartments, or whether VeA can interact with different proteins at different times and places (see below).

## PHOTOLYASE/CRYPTOCHROME: FROM DNA REPAIR TO PHOTOPERCEPTION

Ultraviolet light is harmful to organisms because it leads to DNA damage, such as pyrimidine dimerization. Photoreactivation describes the repair of these lesions by flavoproteins called photoreactivating enzymes (photolyases) that use a blue-light photon as a cosubstrate (109). Cryptochromes (CRY) are photolyase-like blue-light receptors that mediate light responses different from a DNA-repair function and belong also to the photolyase/cryptochrome family. Cryptochrome was initially identified in plants and harbors flavin (FAD), pterin, and deazaflavin as possible chromophores (80). In organisms such as mammals and insects, cryptochromes are related to the metabolic and endocrine circadian clocks (37, 51).

A gene encoding a cryptochrome was identified in the genome of *N. crassa* and other fungi (**Figure 4**). The *N. crassa* cryptochrome CRY-1 is a member of the subfamily CRY-DASH, enzymes with single-stranded DNA-specific photolyase activity (117). Although it was demonstrated that the protein is able to bind single- and double-stranded DNA and RNA, there is no evidence for in vivo photolyase activity (41). The subfamily CRY-DASH also shows transcriptional repressor activity (19), and it has been proposed that CRY-1 of *N. crassa* functions as a modulator of the transcriptional activity of the WCC in the case of some photoactivated genes such as *con-10* (97). The *cry*-1 transcript and the CRY-1 protein levels are strongly induced by blue light in a *wc*-1-dependent manner and are regulated by the circadian clock. However, the light regulatory functions of CRY-1 are still unclear (41).

**DASH:** photolyase/cryptochrome subfamily derived from *Drosophila*, *Arabidopsis*, Synechocystis, human

In *A. nidulans* a photolyase/cryptochrome has been characterized recently (8). Sequence analyses and enzyme activities suggest CryA to be a photolyase. Deletion of the corresponding gene *cryA* stimulated sexual fruiting body formation and caused the induction of regulatory genes of the sexual cycle. CryA thus acts as a repressor of sexual reproduction under ultraviolet light (350–370 nm) and blue light (450 nm). The enzyme also has DNA-repair activity and is thus the first combined cryptochrome/photolyase (8).

## OPSIN: GREEN-LIGHT SENSING?

Rhodopsins are membrane-embedded seven-transmembrane helices photoreceptors composed of a retinal chromophore bound to an opsin apoprotein. Fungal opsins have been described in ascomycetes and basidiomycetes, and sequence similarities have allowed the distinction of three groups of the ascomycetous opsins (**Figure 4**) (18): (*a*) a group similar to the *Leptosphaeria maculans* proton-pumping opsin; (*b*) a group similar to the sensory opsin from *N. crassa*, which are expected to be slow-cycling photosensors; and (*c*) a group of opsin-like proteins. A lateral gene transfer event from haloarchaea into the ancestor of ascomycetes and basidiomycetes has been proposed to describe the evolutionary origin of fungal opsins (107). The third group (opsin-like proteins) does not contain any members characterized biophysically and comprises what is called auxiliary opsin forms, which are present in many fungal species.

Opsin genes have been partially studied in *N. crassa*, *Fusarium fujikuroi*, *A. nidulans* (J. Rodriquez-Romero, M. Hedtke, C. Kastner, S. Müller & R. Fischer, unpublished results),

*C. neoformans*, and *Ustilago maydis* (13, 14, 34, 35, 57, 97). In all cases, no obvious phenotypes were observed after inactivation of the genes, although there is evidence for a function of NOP-1 in the regulation of *N. crassa* development. In *A. nidulans* and other fungi, an open question concerns the retinal because a functional carotinoid biosynthesis pathway is apparently missing. If opsins play a light-regulatory role in fungi, it will be most interesting to see if and how they interact with the other light-sensing systems.

## PHYTOCHROME AND RED-LIGHT PERCEPTION

Although most fungi respond well to blue light, examples for additional red-light sensing were described more than 30 years ago. In *Botrytis cinerea* and *Alternaria solani*, sporulation is inhibited by blue light but the effect could be reverted by red-light illumination (83, 124). Another prominent example is provided by *A. nidulans* (**Figures 2** and **5*a***): In 1990, photobiological experiments suggested that the red-light response may involve a phytochrome (90). However, the dogma at that time was that phytochromes are plant-specific molecules. In 2005 the first fungal phytochromes were characterized (15). A few years earlier, Lamparter & Marwan (73) found spectroscopic evidence in *Physarum polycephalum* for a phytochrome-like protein, although a molecular analysis had not been performed. Phytochromes are meanwhile found in most fungal genomes (**Figures 4** and **6*a*,*c***). Although some fungi contain two copies, many have a single one, but only in some cases has a molecular analysis been performed. In light and dark conditions in *A. nidulans*, conidiation was slightly reduced in a Δ*fphA* strain in comparison to wild type (**Figure 5*b***). This implicates FphA in the control of asexual development. The *fphA* mutant's response to light suggested the presence of other photoreceptors. Likewise, the Δ*lreA*/Δ*lreB*/Δ*fphA* triple mutant caused a drastic decrease of the number of conidiospores in light (**Figure 5*b***).

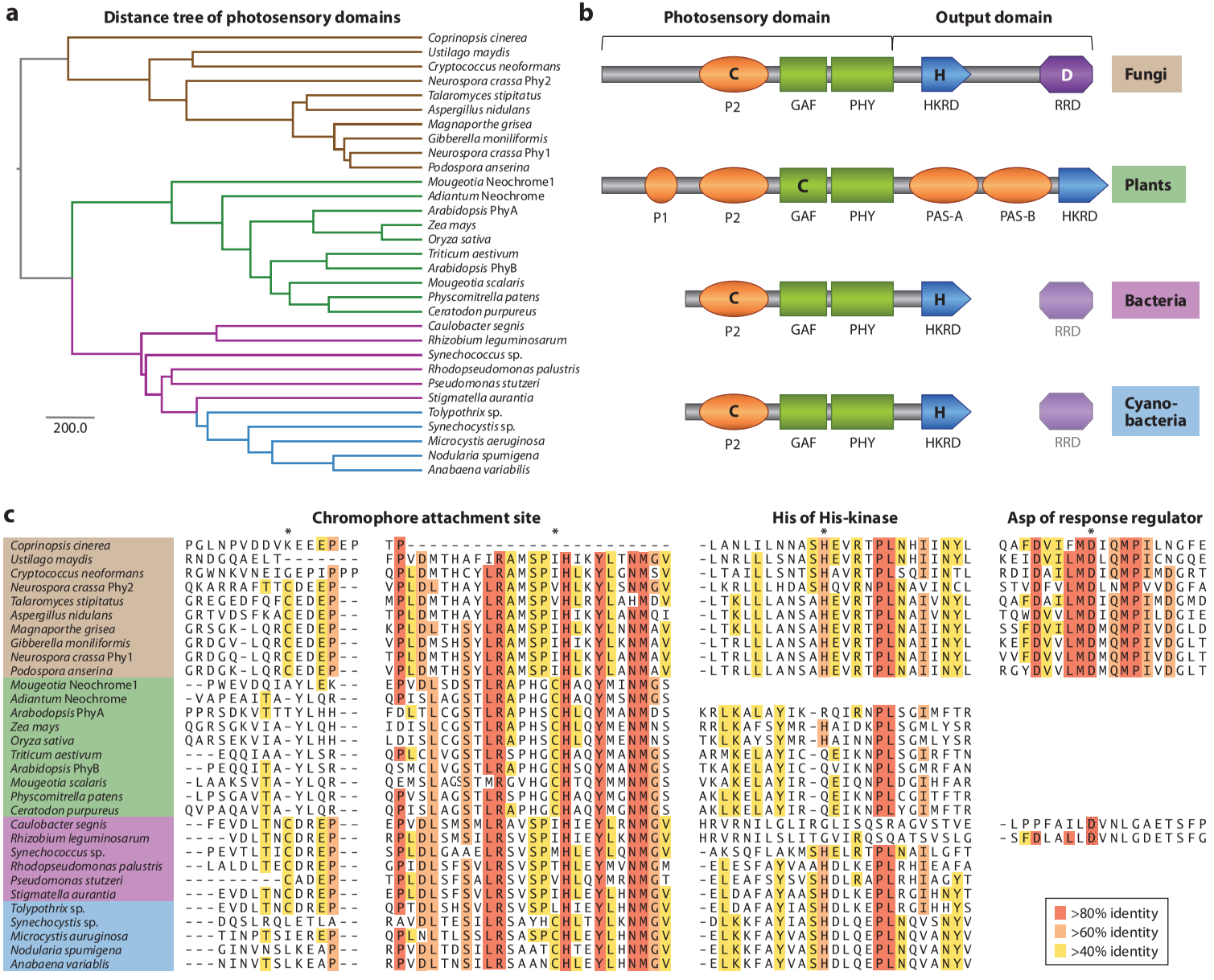
In *A. nidulans*, the number of cleistothecia was slightly induced in the phytochrome mutant in light in comparison to wild type. An almost complete loss of cleistothecium formation was observed in Δ*lreA* or Δ*lreB* strains in light. This loss was largely suppressed by deletion of *fphA*. Double and triple mutants of *lreA*, *lreB*, and *fphA* incubated in light produced the same number of cleistothecia as in the dark. These results demonstrate a repressing function for phytochrome and an activating function for the WC orthologs for the formation of cleistothecia (**Figure 5*b***). In *N. crassa*, deletion of the two phytochrome genes does not cause any obvious phenotype (44). Recently, the involvement of Phy2 as a modulator of the WCC has been shown (97).

### Phytochromes Are Molecular Light Switches with Modular Architecture

Plant phytochromes are soluble chromoproteins that are synthesized in the cytoplasm as ≈120-kDa monomers (102, 104). They contain a linear tetrapyrrol as chromophore, which is autocatalytically attached to a conserved cysteine (**Figure 6*c***). The receptor exists in two convertible forms that are distinguished by their absorption maxima and structure. They are synthesized in the red-absorbing Pr conformation. Absorption of red light first leads to conformational changes of the chromophore followed by changes of the

**Figure 6**

Comparison of fungal, plant, and bacterial phytochromes. (*a*) Average distance tree deduced from an alignment of the photosensory domains. The alignment was made with Clustal W2. The tree was calculated with JalView using the BLOSUM62 matrix. (*b*) Comparison of the domain structures of phytochromes from different groups. ⟨(C)⟩ indicates a conserved Cys responsible for chromophore binding, ⟨(H)⟩ represents the His-residue that is phosphorylated, and ⟨(D)⟩ is the Asp to which the phosphate is subsequently transferred. (*c*) The corresponding alignments. Asterisks indicate amino acids of interest.



protein conformation. The structural changes are accompanied by a shift of the absorption maxima, from red (≈660 nm) to far red (≈730 nm) in the Pfr form. The Pfr form can also absorb far red light by returning to the Pr form. The ratio between these states determines the signaling state of the phytochrome. In most cases, responses are induced by red light and reverted by far-red light, leading to the concept that the Pfr form is the biologically active conformation. Most phytochromes are also able to undergo a dark reversion from the active state to the ground state. Often in plants, there are several phytochromes that differ in absorption spectra or light sensitivity (3, 39, 102–104).

**GAF:** vertebrate cGMP-specific phosphodiesterases, cyanobacterial adenylate cyclases, and formate hydrogen lyase transcription activator FhlA; characteristic of all phytochrome photoreceptors

**PIF:** phytochrome-interacting factor

**HKRD:** histidine kinase–related domain

Phytochromes are proteins with a modular architecture consisting of an N-terminal photosensory module (GAF and PHY domain) harboring the open-chain tetrapyrrol chromophore (**Figure 3**). The GAF domains in plant phytochromes (cGMP phosphodiesterase/adenylate cyclase/Fhl1) binds the bilin; therefore, it is sometimes referred to as bilin lyase domain. In bacteria and fungi, however, the chromophore is attached to a PAS domain designated as the P2 domain (**Figures 3** and **6*b***). The C-terminal output domain varies strongly among different species but always contains a histidine kinase–related domain (HKRD) that is involved in the regulatory output. Plants contain two additional regulatory PAS domains. Depending on the phytochrome subfamily, the nature of the chromophore differs. Whereas plant and cyanobacterial phytochromes incorporate phytochromobilin and phycocyanobilin, respectively, bacteriophytochromes and fungal phytochromes bind the more-oxidized biliverdin IXα. The common feature of these molecules is the ability to absorb red and far-red light, which leads to a *Z-E* isomerization around the C15-C16 double bond. The supply of the bilin chromophore is achieved in several steps. The oxidative cleavage of the precursor molecule heme is performed by a heme oxygenase and leads to the synthesis of biliverdin. For the synthesis of phytochromobilin and phycocyanobilin, an additional reduction step catalyzed by a bilin reductase is needed. Because no heme oxygenase can be identified in most of the currently available fungal genomes, the nature and synthesis of the bilin chromophore remains cryptic (**Figure 4**). In *Saccharomyces cerevisiae* and *Candida albicans*, heme oxygenases are used to acquire free iron from heme, a process necessary for survival and virulence (68, 98). However, these fungi do not possess phytochrome.

## Phytochrome Signaling in Plants

Most phytochrome responses are a result of differential gene expression. Therefore, one crucial step in phytochrome signaling is the transfer of the light signal into the nucleus where gene expression takes place. Plant cytoplasmic phytochrome then shuttles to the nucleus after illumination. This was shown for PhyB, one of the five phytochromes of *Arabidopsis thaliana* (108). There is evidence that an interaction between the N and the C terminus masks a nuclear localization signal in the C terminus, which becomes exposed after irradiation (92, 93). Interestingly, the N terminus alone was sufficient to initiate PhyB-dependent light signaling when targeted to the nucleus (85).

In contrast to PhyB, PhyA does not contain an obvious nuclear localization signal, which suggests different signaling mechanisms. Recent publications suggest that PhyA is transported to the nucleus as a protein complex together with the two proteins Fhy1 and Fhl (56, 106).

Once in the nucleus, phytochrome interacts with transcription factors, such as the helix-loop-helix transcription factor PIF3 (phytochrome-interacting factor 3) (96). PIF3 binds to PhyA and PhyB. Six additional PIFs have also been identified, all highly similar in sequence and structure to PIF3 (25, 78). PIFs predominantly act as negative regulators. In some cases, they accumulate in the dark and are degraded upon illumination by the ubiquitin-26S proteasome system. At least for PIF1 and PIF3, the degradation depends on direct interaction with the phytochrome molecule and is induced by protein phosphorylation (7, 25, 89, 118).

## Plant Phytochromes as Light-Regulated Kinases

Besides the important light-dependent nuclear shuttle mechanism, phytochrome may also act as a light-modulated kinase (**Figure 7*a***). As one common structural feature, phytochromes contain an HKRD in their C terminus (**Figure 6*b***). However, plant phytochromes are not active histidine kinases (HKs) because they lack the critical histidine residue required for autophosphorylation. Hence, the HKRD of plant phytochromes is considered to be an evolutionary remnant of a bacterial ancestor phytochrome. Plant phytochromes may show Ser/Thr kinase activity rather than HK activity, and Pfr seems to be the active form (130). Different light-dependent phosphorylations within the N terminus (Ser7/17) and in the hinge region (Ser598) have been identified (76, 86). Because the phosphorylation at Ser598 prevented the interaction between PhyA and its putative signal transducers nucleoside diphosphate kinase 2 and PIF3, Ser598 is thought to be involved in an inhibitory mechanism (70). Recently, autophosphorylation sites were mapped in the N-terminal extension region, playing an important role in the regulation of oat phytochrome signaling through the control of phytochrome stability (48).

Phosphotransfer has been observed from PhyA to the phytochrome kinase substrate 1 (PKS1) in vitro. The residues phosphorylated in PKS1 were Ser and Thr, and the Pfr form of PhyA appears to be more active than the Pr form in phosphotransfer. PKS1 binds to the C-terminal part of phytochromes. Although Pr and Pfr have different protein conformations, PKS1 appears to bind both spectral forms. PKS1 acts as negative regulator of phytochrome function (40), and it is still under discussion whether PKS1 is the cytoplasmic retention factor preventing phytochromes from migrating into the nucleus (38).

## Bacterial Phytochromes as Light-Regulated Histidine Kinases

A new impetus toward phytochrome research was provided by the discovery of phytochrome-like sequences in photosynthetic bacteria as well as in nonphotosynthetic prokaryotes (12, 65). The cyanobacterial phytochrome Cph1 from *Synechocystis* sp. *PCC6803* shows striking similarity to plant phytochromes and is closely related to sensor HKs (88) (**Figure 6*b***). In contrast to plant phytochromes, Cph1 is a light-regulated HK that performs autophosphorylation and transphosphorylation to an aspartate in its potential response regulator Rcp1. Both processes are stimulated by far-red light and inhibited by red light. Thus, *Synechocystis* phytochrome works contrary to plant phytochromes, with the Cph1-Pr form representing the active kinase (131). However, recent publications showed that Pfr dimers are more stable than Pr dimers and the Cph1-Pr form is considered to be the ground state (33, 123).

*Agrobacterium tumefaciens* is a nonphotosynthetic soil-born bacterium that contains two phytochromes called Agp1/2 that covalently attach biliverdin within their N-terminal chromophore-binding domain (61, 74). Agp1 behaves like a typical bacterial phytochrome: The form initially synthesized is Pr and can be converted by red light to the unstable Pfr form (dark reversion to Pr). Agp1 contains an HK domain and appears to be encoded in an operon together with a response regulator of the CheY superfamily (AtRR1) and another open reading frame designated ExsG that encodes a protein with an N-terminal response regulator (RR). In addition, Agp1 functions as a light-regulated HK (74). Co-incubation of phosphorylated Agp1 with its associated AtRR1 allowed the transfer of the bound phosphate to the RR. Kinase activity of Agp1 is repressed after photoconversion to Pfr, which suggests Pr is the active form (64). This is in contrast to plant phytochromes, which are considered active in the Pfr state. The organization and the activity of Agp2 are different from those of Agp1. The region adjacent to the chromophore-binding domain comprises a domain that is weakly related to two-component HKs and ends in an RR domain. The spectral form initially observed is Pfr, and in protein kinase assays, Pfr was more active than was Pr. Thus, both *Agrobacterium*

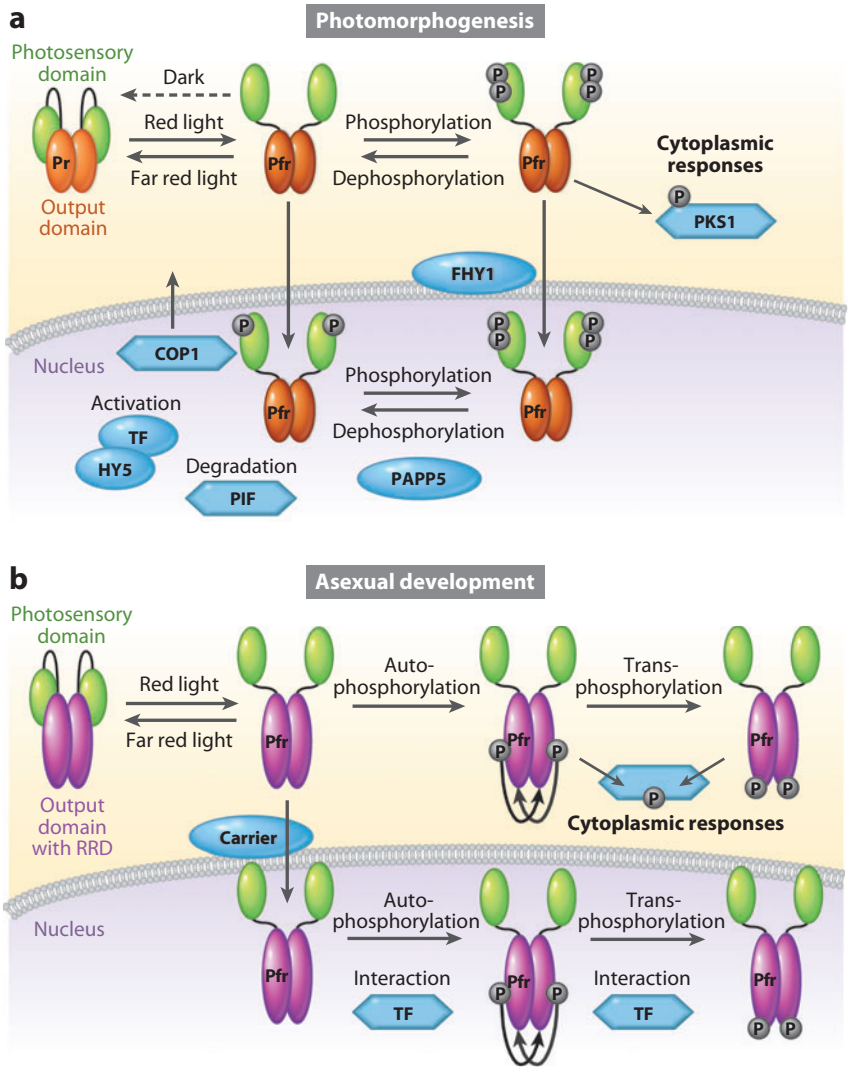
**RR:** response regulator

phytochromes show opposite photobiology and could function as opposing light sensors (64).

For most bacterial phytochromes, the events following RR phosphorylation remain unclear. Phosphorylated RRs may either directly interact with their targets or participate in a four-step phosphorelay His→Asp→His→Asp before the signal output (126). Another breakthrough was achieved with the *D. radiodurans* phytochrome, namely the crystallization of the PAS and GAF domains (127). Soon after, Agp1 form *A. tumefaciens* was crystallized (112). For more details on this aspect, readers are referred to Reference 103.

## Fungal Phytochromes as Light-Regulated Histidine Kinases

The first complete phytochrome-like sequences were identified in the first fungal genome sequences of *N. crassa*, *A. fumigatus*, and *A. nidulans* (65). Fungal phytochromes are more closely related to bacterial than to plant phytochromes, which is highlighted by the fact



that a complete output module consisting of an HK and an RR domain is encoded within the same gene as the chromophore-binding domain (65) (**Figure 6*b***). The *N. crassa* genome encodes two phytochromes, PHY-1/2, and both of them contain RR motifs at the C terminus (44). However, only for the *A. nidulans* phytochrome FphA has a light-driven HK activity been determined (16). Previously, it was shown that FphA forms dimers and that a conserved cysteine residue 195 within the PAS domain serves as the chromophore attachment site. After binding to biliverdin, FphA shows the spectral properties typical of a phytochrome (15). Pr is the form initially synthesized in the dark (max 705 nm) that turns into Pfr (max 758 nm) under red-light illumination. Dark reversion has been observed only after deletion of the N-terminal variable extension. In this context, the extension comprising the first 172 amino acids is sufficient to stabilize the Pfr form of FphA (16). In protein kinase assays, a light- and chromophore-dependent phosphorylation of both Pr and Pfr was observed, but initially the signals could not be clearly assigned to either auto- or transphosphorylation (15, 16) (**Figure 7*b***). Recently, Brandt et al. (16) found strong red-light-dependent autophosphorylation activity for FphA. Thus, the Pfr form appears to be an active HK, but autophosphorylation of the Pr form could also be observed and depends on a functional RR domain of the dimerization partner. These data suggest a functional RR domain is necessary for tuning the kinase activity in both spectral forms. Subsequently, a phosphotransfer from the HK to the RR domain of the dimerization partner occurs in a process independent of the bound chromophore in the phospho-accepting RR domain. Thus, transphosphorylation also occurs within heterodimerization of holo- and apo-FphA variants (16). Very likely, a phosphotransfer initiated from the sensor HK FphA plays a role in further light-signaling cascades.

Accordingly, the identification of FphA-interacting proteins appears to be crucial to better understand the signaling process. Those proteins have been identified in two different approaches: In a targeted approach, using the split YFP system and Co-IP, our group described a light-regulator protein complex

**Figure 7**

Simplified scheme of light signaling in plants (*a*) and fungi (*b*). As with **Figure 6,** the following color code was used: The N-terminal photosensory domain is shown in green and the C-terminal output domain is shown in orange and purple. (*a*) In the inactive Pr form the N- and C-terminal halves of the phytochrome interact with each other and red-light illumination causes structural changes that result in the active Pfr form. Light-dependent phosphorylation is achieved either by an unidentified kinase or/and by an autophosphorylation mechanism. PKS1 is one target of the phytochrome phosphotransfer and is probably involved in the cytoplasmic output. The light response involves the shuttle of phytochrome to the nucleus, where interactions between Pfr and transcription factors take place. Phytochrome-interacting factors (PIFs) are negative regulators, and Phy-dependent degradation of these transcription factors causes the photoresponse. COP1 is a master repressor of photomorphogenesis and mediates degradation of positive factors, such as HY5, selectively in the dark. Phytochrome inhibits COP1 activity by excluding COP1 from the nucleus (exposure to light reduces the nuclear abundance of COP1, thereby presumably reducing the rate of HY5 protein degradation and allowing HY5 to accumulate in the nucleus). Dephosphorylation of the phytochrome by the phosphatase PAPP5 enhances the stability of the light sensor and facilitates phytochrome mediated responses (see Reference 3). (*b*) Hypothetical model of light signaling in *Aspergillus nidulans*. Red-light illumination of the Pr form leads to conformational changes in the phytochrome protein, and the resulting Pfr is regarded as the active form. Pfr is autophosphorylated at a conserved His in a histidine kinase-related domain and is able to transphosphorylate an Asp of the response regulator (RR) domain (*shown in purple*) in the neighboring dimerization partner. Downstream targets of the phosphorylated RR domain are not yet known. The mechanism of nuclear import is not known and may be supported by carrier proteins. In the nucleus, FphA interacts with transcription factors that could be negative or positive regulators of asexual and/or sexual development.

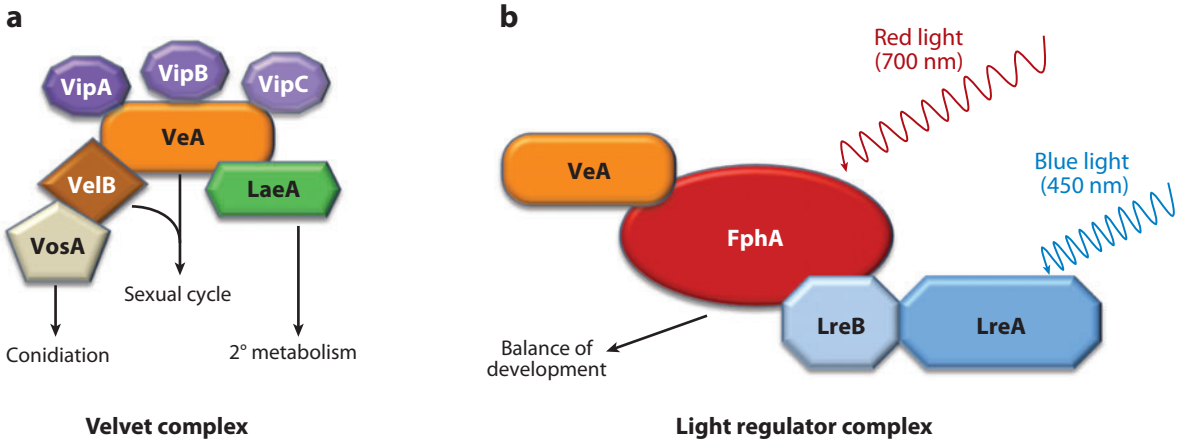



**Figure 8**

Scheme of two different protein complexes related to light regulation identified in (*a*) Velvet complex (9) and (*b*) Light-regulator complex (101). See text for details.



consisting of the WC homologs, LreA and LreB as well as FphA and VeA (101). FphA appeared to interact directly with VeA and LreB (**Figure 8*b***). The interactions were mapped to the C-terminal output motif of FphA and VeA was found to be a highly phosphorylated protein (100), although no downstream phosphotransfer initiated by FphA was shown. Interestingly, the interactions occurred in the nucleus although the phytochrome protein is mainly found in the cytoplasm. Similar to the situation in plants, a nuclear shuttle should occur at some point. The fact that under all conditions large amounts of the protein were found in the cytoplasm could be due to moderate overexpression of the protein in those experiments, but it could also indicate a cytoplasmic besides the nuclear function. Indeed a light-dependent nuclear shuttle of VeA has been reported, which could be crucial for, e.g., the regulation of the FphA activity in the nucleus (23, 121).

Further evidence for the involvement of the *A. nidulans* phytochrome in a phosphorelay system came from the observation of a retrograde phosphotransfer from the phosphotransmitter YpdA to the conserved aspartate in the RR domain of FphA (2). Yet, it is unclear how the interacting proteins influence the activity of the sensor HK FphA.

In a TAP-tag approach, Bayram et al. identified a second protein complex that contains the VeA protein (9) (**Figure 8*a***). However, in this approach FphA, LreA, and LreB were not identified, suggesting VeA is a partner of two distinct protein complexes.

## The Response Regulator Receiver Domain of Phytochromes

A striking feature of fungal phytochromes is a RR receiver domain at the C terminus (**Figures 3** and **6*b***). RR were thought to be unique to bacteria but have now been identified in fungi and plants (91). Proteins with this domain are involved in phosphotransfer pathways and signal transduction. Bacterial RRs and their mode of action have been studied extensively since the 1980s (59, 129). RRs are part either of a two-component system, often encountered in prokaryotes, or of a more complex phosphorelay system, which is predominantly, but not exclusively, found in eukaryotes (122). Two-component systems consist of two distinct proteins, an HK and an RR, which often acts as a transcription factor. In eukaryotic phosphorelay systems, the sensory molecule is called a hybrid kinase because the protein harbors a HK domain and a C-terminal RR receiver

**Phosphorelay system:** complex variant of a bacterial signaling system, where a phosphotransfer intermediate carries a phosphate from a hybrid sensor HK to a RR

domain. The RR has no effector domain but accepts and transmits only the phosphoryl group from the HK domain to a histidine-containing phosphotransfer protein (HPt) that interconnects the hybrid kinase with another RR. This terminal RR comprises an effector domain and promotes the response to the stimulus, for example, by binding to DNA and regulating gene expression. RRs are acceptors for a phosphoryl group that is transferred from a conserved histidine in the kinase domain to a conserved aspartate in the receiver domain of the RR. This transfer is catalyzed by the RR (45).

Fungal phytochromes such as FphA from *A. nidulans*, Phy-1/2 from *N. crassa*, and Phy1 from *C. neoformans* are hybrid kinases that are presumably part of a phosphorelay system. Their RR receiver domain is structurally similar to CheY. CheY-like RRs are small molecules (150 amino acids) (1). In *Escherichia coli*, the response to the stimulus is achieved through binding of phosphorylated CheY to flagellar motor proteins.

Bacteriophytochromes and cyanobacterial phytochromes are classical two-component systems apart from a few exceptions such as BphP2 (Agp2) from *A. tumefaciens* (see above). The corresponding RRs of these phytochromes also belong to the CheY superfamily.

Because the RRs associated with fungal phytochromes do not have a C-terminal output domain, the mode of action of the fungal phytochromes still remains unclear. The questions of how the photoreceptor regulates gene expression and which proteins are involved in this process remain unanswered.

## INDENTIFICATION OF LIGHT-REGULATED GENES

Many light responses, in plants as well as in fungi, suggest massive differential gene expression. To date, a few light-regulated genes have been identified and characterized. Examples are the *albino* genes of *N. crassa* (see above): *ccg-2*, *con-10*, *con-6*, and *vvd* (54, 82). In *T. atroviride*, regulation of the expression of the photolyase gene *phr-1* is light inducible (10, 11), and in *T. reesei*, light stimulates cellulase gene expression (113). The availability of genome-wide expression profiling tools and the advent of the pyrosequencing technology recently allowed global analyses and provided many novel insights. These analyses have been performed mainly in the three ascomycetes *N. crassa*, *T. atroviride*, and *A. nidulans*.

Initially, using spotted microarrays of *N. crassa*, Lewis et al. (79) found that about 3% of all genes were regulated by light (94). Most recently, a complete analysis has been performed with an Affymetrix microarray system and the number of blue-light regulated genes was estimated at 6% (26).

Light-induced genes were initially classified into three classes based on their expression profiles (79). Class I genes, including *vvd* and *con-10*, were rapidly induced by light, reaching peak levels 30–60 min after transfer to constant light and returning to low levels after 120 min of light exposure. Class II genes, including *con-6*, were induced more gradually. These genes peaked 60–120 min after transfer to constant light and began to decline after 240 min following exposure to light. Class III genes, including *ccg-2*, showed an early peak at 60 min, reduced mRNA levels at 120 min, and then increased levels at 240 min after light induction. Class I and II genes showed light-adaptation responses, and transcription was induced only transiently in response to the light signal. This pattern of regulation is typical for most known light-regulated genes, supporting the existence of a general mechanism that allows cells to adapt to a light stimulus (115, 119). However, for class III genes, adaptation responses have not been observed. The complex light responses suggest complex molecular mechanisms, with variations among different gene classes and not only on/off responses.

The recent microarray experiments with full-genome coverage (125) and large-scale quantitative analyses have provided a catalog of 314 genes showing strong early or late light responses. Functional and sequence analyses suggested a clear correspondence between the timing of induction and gene functions.

**ELRE (LLRE):** early (late) light-response element

The WCC induces the expression of a first group of genes (first minutes of illumination) by binding to their promoter regions to early light-response elements (ELREs) previously identified as light-response elements (43, 52, 62). The consensus sequence determined using the program SCOPE was bvGATCb (b stands for C, G, or T and v stands for A, C, or G) for the ELREs with coverage of 97.6% of the upregulated genes. Light induction is thus regulated through binding of the light-activated WCC to the corresponding promoters. A second group of genes with a late light response are regulated in part by SUB-1, an early light-responsive transcription factor. SUB-1 recognizes late light-response elements (LLREs) identified in the promoter region of 154 genes, located within the 500 bp upstream of the translation start codon (26). The consensus sequence for the LLRE has been determined to rTGAyrTCA to which the SUB-1 protein is binding.

In *T. atroviriden*, 40 genes regulated by white light have been identified using cDNA microarrays. These represented 2.8% of the genes printed on the array. Thirty genes were up- (2%) and 10 were downregulated (0.8%). All genes are regulated through the WC homologs BLR1 and BLR2 (105). However, expression analyses in *blr*-deletion mutants identified a *blr*-independent response in addition to the expected *blr*-dependent one. Another interesting aspect was a new role of the BLR proteins in the repression of transcription. Recently, 454 pyrosequencing technology has been used to analyze expressed genes (A. Herrera-Estrella, personal communication). A group of 331 light-regulated genes has been identified and compared with the 314 light-regulated genes reported for *N. crassa* (26). Surprisingly, only 26 genes showed the same expression pattern, among them frequency (*frq*), photolyase (*phr-1*), and vivid (*vvd*). The significance of such a low number of genes with similar regulation in the two related fungi remains to be elucidated. In agreement with previous experiments, a number of genes that showed *blr*-independent light-regulation were identified, suggesting the action of other photoreceptors. The promoter region of the genes regulated by blue light through the BLR proteins contain GATA elements, similar to the consensus sequence of the ELRE described in the genes regulated by light in *N. crassa* (53, 105). The analysis of the promoter region of the 331 differential genes identified showed that 209 genes (63%) contain ELREs.

In *A. nidulans*, a two-color microarray system (spotted microarray) has been used for a global analysis of light-regulated genes (J. Rodriquez-Romero, M. Hedtke, C. Kastner, S. Müller & R. Fischer, unpublished data). This fungus deserves special attention because of the pronounced red-light response and the well-documented role of phytochrome in that response. After 30 min of illumination with white light, approximately 260 genes (approximately 2.5% of the whole genome) were differentially regulated; 209 genes were up- and 51 downregulated. Some of those genes displayed homology to other photo-inducible genes identified previously in *N. crassa* such as *ccg-1*, *con-10*, and *con-6*. Some photo-inducible genes encode transcription factors and enzymes probably implicated in the secondary metabolism. Many genes encode proteins involved in stress responses, and a large group represents uncharacterized genes.

Taken together, the global analyses highlight the importance of light regulation in these fungi and suggest that the light signal is used to adapt to the harsh environment encountered by hyphae, which leave a substrate and grow on its surface (**Figure 1**). Such drastic changes in the environment also occur during the night-day cycle for hyphae that grow on a surface. For example, the temperature rises during the day, humidity may decrease dramatically during the day, and reactive oxygen species are produced in high concentrations. As an adaptation to these rhythmic changes, a circadian clock is functional in many fungi. This clock allows fungi (and other organisms with a clock) to foresee the upcoming changes every morning and thus physiologically adapt to the changes before they actually occur and cause damage.

The circadian clock in *N. crassa* is composed of a positive element, the WC proteins, and a negative element, the Frequency protein. Given the apparent advantage of a circadian clock, it is surprising that the key protein, Frq, appears not to be conserved in all fungi (**Figure 4**). However, for example, in *A. nidulans*, evidence for a circadian clock has been provided (46). This suggests a frq-independent clock system. Thus, *A. nidulans* does react strongly to red light but does not contain a Frq ortholog, whereas *N. crassa* does not show a red-light response but contains Frq (**Figure 4**). Whether other fungi whose genomes lack a copy of *frq* also show a red-light response remains to be determined.

## THE CHROMATIC VISION IN FUNGI AND FUTURE PERSPECTIVES

Fungi "see" light and may react with numerous physiological and morphological responses. They employ nearly all known photoreceptors from higher eukaryotes to sense several regions of the light spectrum. The number of responses and the complex regulation pattern of many light-regulated genes suggest an interplay of light receptors with each other and/or with other regulatory proteins in the cell. The output of light sensing is not just a yes or no answer, but it appears as a complex and fine-tuned response. However, it is still too early to develop a general picture. Our knowledge is still fragmentary and many interesting findings have yet to be made. Fascinating aspects include the functional or physical interplay between different photoreceptors and the mechanism of signal transduction from the primary light absorption event of the chromophore to protein conformational changes of the apoprotein leading to protein interactions and gene-expression regulation. Last but not least, the research of light responses in fungi (and bacteria) has changed our view on the evolutionary origin of photoreceptors as demonstrated by phytochrome. This light-sensing system was thought to be confined to plants but its discovery outside the plant kingdom demonstrated its "old" invention during evolution.

### SUMMARY POINTS

1. Light perception in fungi is mainly achieved by flavoproteins, namely White Collar, Vivid, or chryptochrome homologues. In addition, tetrapyrrol-based phytochromes and perhaps retinal-binding opsins are involved in light sensing.
2. DNA binding activity has been shown for some WC proteins. This allows immediate and complex changes of gene expression in response to light.
3. Genes encoding WC homologs are conserved in almost all fungal genomes sequenced so far. They are involved in the regulation of sporulation, development, pigment biosynthesis, and the entrainment of circadian clocks.
4. Although phytochromes are present in the majority of fungal genomes, their function is often unclear. We hypothesize an increasing importance for red-light perception in fungi lacking a frq-based circadian clock.
5. In contrast to plant phytochromes, fungal phytochromes have a functional His kinase domain, which is involved in signaling.
6. The "chromatic" vision in fungi suggests complex interconnections between different photoreceptors to modulate the response as a function of changing light conditions.

### FUTURE ISSUES

1. Possible cross-talk between different light-signaling pathways and the integration of other environmental conditions need to be determined.
2. Further photoresponses, especially for red and green light, are likely to exist and need to be discovered.
3. The impact of light on gene regulation must be understood.
4. The different light-regulation complexes identified to date need to be characterized in terms of their localization, their protein composition, and the light-signaling events within the complexes.

## DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

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