Gene Expression Regulation in Photomorphogenesis from the Perspective of the Central Dogma

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Abstract

Depending on the environment a young seedling encounters, the developmental program following seed germination could be skotomorphogenesis in the dark or photomorphogenesis in the light. Light signals are interpreted by a repertoire of photoreceptors followed by sophisticated gene expression networks, eventually resulting in developmental changes. The expression and functions of photoreceptors and key signaling molecules are highly coordinated and regulated at multiple levels of the central dogma in molecular biology. Light activates gene expression through the actions of positive transcriptional regulators and the relaxation of chromatin by histone acetylation. Small regulatory RNAs help attenuate the expression of light-responsive genes. Alternative splicing, protein phosphorylation/dephosphorylation, the formation of diverse transcriptional complexes, and selective protein degradation all contribute to proteome diversity and change the functions of individual proteins.

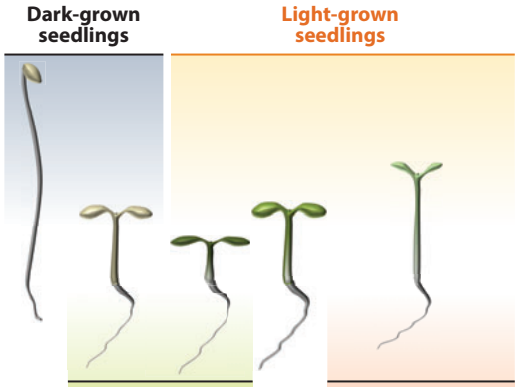
Contents

1. INTRODUCTION

Light is one of most influential environmental stimuli, regulating numerous growth and developmental processes during a plant's life cycle, from seed germination through early seedling establishment, shade avoidance, the establishment of the circadian rhythm, flowering, and eventually senescence (63). Plants possess cryptochromes, phototropins, and phytochromes to perceive and coordinate UVA blue (B) and red/far-red (R/FR) light signals in their living environment. The B and R/FR light photoreceptors have been comprehensively reviewed (22, 86, 96). In addition, UV RESISTANCE LOCUS 8 (UVR8) was recently discovered to be the UVB photoreceptor (111).

When seeds germinate in the soil under darkness, young seedlings undergo skotomorphogenesis and have closed cotyledons, unopened hooks, and elongated hypocotyls (**Figure 1**). Upon protruding from soil, the seedlings proceed with photomorphogenesis, a developmental process that transforms them into a vegetative state that is required for photosynthetic activity. The process of photomorphogenesis, or de-etiolation, has been widely used for studies of light-sensing and signaling pathways. This early seedling development is also modulated by multiple plant hormones (72, 137). Here, I concentrate on regulatory genes that respond to light signals.

Genes contributing to the regulation of photomorphogenesis can be broadly classified as either positive or negative regulators of photomorphogenesis. When seedlings are grown in the light, light inhibits hypocotyl elongation. Mutants defective in positive regulators are less sensitive to light treatment and exhibit a long-hypocotyl phenotype. ELONGATED HYPOCOTYL 5 (HY5) is one of the best-characterized positive regulators of photomorphogenesis (102). However, mutations in negative regulators of photomorphogenesis lead to photomorphogenic development when seedlings are grown in the dark or show hypersensitivity to light (shorter hypocotyls as compared with wild-type seedlings). CONSTITUTIVE PHOTOMORPHOGENIC 1 (COP1) is one such negative regulator (31).



	Wild type	Negative-regulator mutant	Wild type	Positive-regulator mutant
Photoreceptors				*phyA, phyB, cry1, cry2*
Chromatin remodeling enzymes		*hd1/hda19, epp1/pkl*		(*taf1*), *gcn5, hda15*
Transcription factors		*pifq, bbx24, bbx25, gbf1, bzip16, zbf1*		*hy5, hyh, hfr1, laf1, pat1, fhy3, far1, bbx4, bbx20, bbx21, bbx22, gata2*
Splicing factors		*skip*		*rrc1*
Actions of microRNAs		*ago1* (?)		
Translation factors		*eif3h*		
Protein degradation factors		*cop/det/fusca, spa, pks1, eid1*		*afr, max2/ore9*

Figure 1

Photomorphogenic mutants included in this review. Skotomorphogenic and photomorphogenic development of the wild type and mutants of positive and negative regulators are shown. Mutants are categorized by their roles as positive or negative regulators and their contributions at different levels of gene expression regulation.

The switch from skotomorphogenesis to photomorphogenesis is the conclusion of tightly regulated gene expression and the interaction of gene products. A broad definition of gene expression involves producing functional RNA and/or protein products from the genetic codes. This article focuses on light-regulated gene expression at various levels of the central dogma, including transcriptional, posttranscriptional, translational, and posttranslational regulation. **Figure 1** lists the key regulators highlighted in this article.

2. TRANSCRIPTIONAL REGULATION

Light triggers the targeting of the phytochrome (phy) R/FR-light photoreceptors and the UVR8 UVB photoreceptor to the nucleus (23, 36, 62). The cryptochrome (cry) B-light photoreceptors are also present in the nucleus (138, 145). Genetic screens have yielded many *Arabidopsis thaliana* mutants with aberrant photomorphogenic phenotypes (24). Like photoreceptors, the protein products of many of the genes identified in mutant screens are localized in the nucleus. The localization of photoreceptors and light-signaling molecules within the nuclei suggests active molecular modulation within the nucleus, including the modification of chromatin structures and

changes in transcriptional activities. These events contribute to the transcriptomic adjustment in photomorphogenic *Arabidopsis*.

2.1. Chromatin Remodeling for Light-Regulated Gene Expression

The chromatin structure—including nucleosome positions and compaction—on the promoter region of a gene can affect its transcription activity. Posttranslational modifications of the N-terminal tails of histones in the nucleosome can affect nucleosome position and density. The most commonly seen modifications of histones include acetylation, methylation, phosphorylation, and ubiquitination.

2.1.1. Histone modification and expression of light-regulated genes. Among the histone modifications, hyperacetylation can help to relax chromatin structure and lead to transcriptional activation (70). In pea, light upregulation of the plastocyanin gene *PetE* is associated with the hyperacetylation of histones H3 and H4 in a light-dependent manner (25, 26). Light also triggers the acetylation of histone H3 on lysine 9 (H3K9) and histone H4 on lysine 5 (H4K5) in the promoter and transcribed region of the C_4-specific phosphoenolpyruvate carboxylase gene *C_4-Pepc* (99, 100).

The level of chromatin compaction differs among *Arabidopsis* accessions but is associated with the light intensity of the native habitats of these accessions (132). Changes in light quality and quantity also influence histone modifications, especially H3K9 acetylation, in *Arabidopsis* seedlings (42). This study additionally showed that photoreceptors and key regulators, including COP1 and HY5, are involved in the changes in histone modifications and the association of RNA polymerase II with light-responsive genes (42).

In contrast, specific histone trimethylations can repress transcription. Quick light-repressed expression of *PHYA* was accompanied by an increase in H3K27 trimethylation and a decrease in H3K9/14 acetylation and H3K4 methylation levels surrounding the translation start site (54) (**Figure 2*b***). A genome-wide survey of four histone modifications (H3K9 acetylation, H3K9 trimethylation, H3K27 acetylation, and H3K27 trimethylation) provided a more comprehensive picture of global histone modification in de-etiolating *Arabidopsis* seedlings (20). This study revealed a clear and dynamic association between H3K9 acetylation and the gene expression of *HY5*, *HYH*, and photosynthesis-related genes (20).

2.1.2. Photomorphogenic development of chromatin-modifier mutants. Previous studies have identified chromatin-modifying enzymes responsible for the diverse and dynamic modifications of histones. Genetic studies in *Arabidopsis* further supported the idea that changes in histone codes are involved in photomorphogenesis (**Figure 2*b***). An *Arabidopsis* mutant defective in the histone acetyltransferase HAF2/TAF1 showed light-insensitive phenotypes, including reduced expression of light-responsive genes and decreased accumulation of chlorophyll (7). The *haf2/taf1* mutant showed reduced acetylation of histones H3 and H4 in the *RBCS-1A* promoter and histone H3 in the *CAB2* promoter, in addition to their reduced expression (7). Similarly, mutation in another histone acetyltransferase, GCN5, produced a long-hypocotyl phenotype in light with reduced H3K9, H3K27, and H4K12 acetylation on promoters of target genes (5). Although a genome-wide search of GCN5 target genes did not reveal a preferential binding of GCN5 to light-upregulated genes, the binding of GCN5 and HY5 to the promoter was proposed to prime the activation of early light-responsive genes (6).

Mapping of quantitative trait loci revealed that *HISTONE DEACETYLASE A6* (*HDA6*) and the polymorphic alleles of *PHYB* play positive roles in light-regulated chromatin compaction

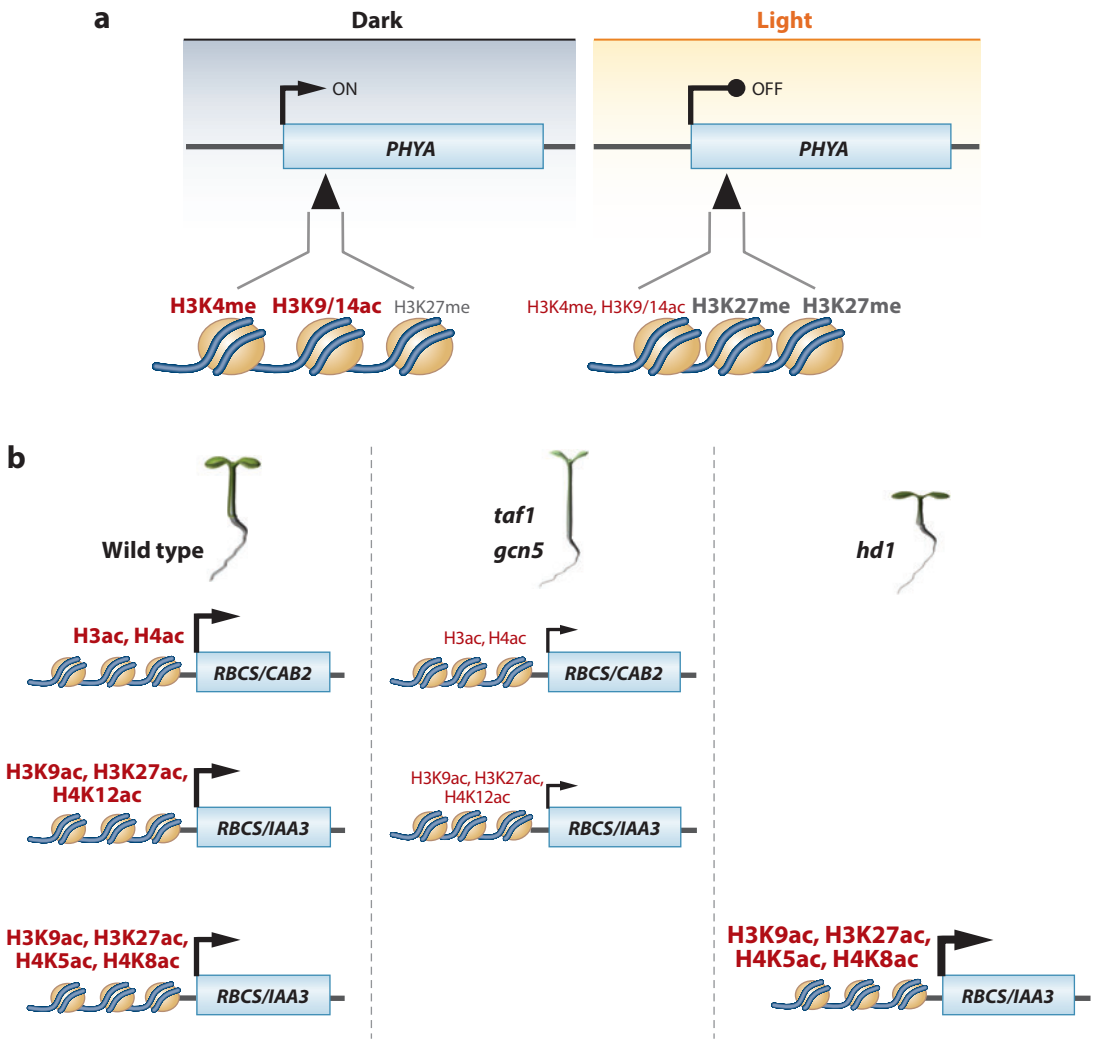


Figure 2

Examples of changes in light-regulated gene expression due to chromatin modifications (ac, acetylation; me, methylation). (*a*) Expression and chromatin modifications of *PHYA* under dark or light conditions. The filled triangles indicate the translation start. Histone modifications in red and gray text indicate modifications for turning gene expression on and off, respectively. (*b*) Expression and chromatin modifications of *RBCS-1A*, *CAB2*, and *IAA3* in the wild type and in *Arabidopsis* mutants defective in chromatin-modifying enzymes. Thicker arrows indicate stronger expression. Font size positively correlates with the degree of histone modification indicated.

(132). Benhamed et al. (5) showed that HD1/HDA19 functions to repress the acetylation of H3K9, H3K27, H4K5, and H4K8 of light-responsive genes, which explains in part the light-hypersensitive phenotype in the *hd1* mutant. HD1/HDA19 also regulates the deacetylation of H3K9/14 on the *PHYA* locus (54). In contrast, *Arabidopsis* plants defective in *HDA15* showed longer hypocotyls under R/FR light, indicating that HDA15 is a positive regulator of R/FR-light-signaling pathways (84). Interestingly, in the dark, HDA15 also functions to repress the expression of genes in chlorophyll biosynthesis and photosynthesis by decreasing the acetylation levels in these genes (84). The HDA15-dependent deacetylation of these genes depends on a negative regulator

of photomorphogenesis, PHYTOCHROME INTERACTING FACTOR 3 (PIF3), possibly by protein–protein interactions (84).

Another negative regulator of photomorphogenesis is PICKLE (PKL)/ENHANCED PHOTOMORPHOGENIC 1 (EPP1), an ATP-dependent chromatin remodeling factor from the chromodomain/helicase/DNA-binding family (59). In the dark, PKL/EPP1 can be recruited to promoters of cell-elongation genes by the transcriptional regulator HY5 and function to repress H3K27 trimethylation levels, thus leading to the expression of these genes and cell elongation (59). Light downregulates the expression of *PKL/EPP1* and stabilizes HY5 (see below), which increases H3K27 trimethylation levels and represses cell-elongation gene expression in photomorphogenic development (59).

Ubiquitination is another form of histone modification. In the early photomorphogenic stage, light induces a quick redistribution of the monoubiquitinated histone H2B marks in the *Arabidopsis* genome (10). As compared with its genome-wide distribution, modification of monoubiquitinated histone H2B is overrepresented in coding regions of genes upregulated by light, especially those that play important regulatory roles in photomorphogenesis (10).

2.2. Positive and Negative Transcriptional Regulators in Photomorphogenesis

Both classical and reverse genetic approaches have been broadly used for identifying genes that when mutated result in aberrant photomorphogenic phenotypes. These approaches have yielded many *Arabidopsis* mutants defective in transcriptional regulators, primarily in the families of B-box zinc-finger transcription factors (BBXs), basic helix-loop-helix transcription factors (bHLHs), and basic region/leucine zipper motif transcription factors (bZIPs).

2.2.1. B-box zinc-finger transcription factors. Many BBXs are important regulators in photomorphogenesis (11, 65). Among them, BBX4/COL3, BBX20/BZS1, BBX21/STH2, and BBX22/LZF1 are positive regulators (18, 28–30, 35). BBX22, a direct target of HY5, positively regulates genes involved in the biosynthesis of anthocyanin and the biogenesis of chloroplasts (18). In contrast, BBX24/STO and BBX25/STH negatively regulate photomorphogenesis by interfering with the transcriptional activity of HY5 toward BBX22 (39).

2.2.2. Basic helix-loop-helix transcription factors. PIF3 was the first bHLH transcription factor identified to regulate photomorphogenesis in *Arabidopsis* (97). The involvement of multiple PIFs in photomorphogenesis and their molecular actions have been comprehensively reviewed (3, 17, 57, 76) and are not elaborated here. More recently, the transcriptomic impact of PIF1, -3, -4, and -5 and their direct genomic targets were surveyed on a genome-wide scale (77, 147). The *cis*-elements G box (CACGTG) and PBE box (CACATG) were found to be enriched in direct target genes of PIFs (147). PIFs function in a partially overlapping way, but each PIF has a different molecular effect (77). Results have also indicated that PIFs and phytochromes antagonistically regulate transcriptomic alteration (77).

LONG HYPOCOTYL IN FAR-RED 1 (HFR1) is an atypical bHLH and a positive regulator of the phyA-signaling pathway (34). Another bHLH, the Z-box binding factor ZBF1/MYC2, is a negative regulator of photomorphogenesis (140).

2.2.3. Basic region/leucine zipper motif transcription factors. In the bZIP family, HY5 (21) and its homolog HYH (47) are the members that have been most extensively characterized for their positive roles in photomorphogenesis. HY5 and HYH belong to group H of the bZIP family. HY5 contributes broadly to actions of various wavelengths of light and the integration of light- and

hormonal-signaling pathways (72). HY5 initiates a transcriptional cascade by directly targeting the promoters of thousands of genes (41, 146).

In group G of the bZIP family, the G-box binding factors GBF1, -2, and -3 can bind to the *cis*-element G box (CACGTG) in promoters of light-responsive genes (115). During photomorphogenic growth, GBF1 negatively regulates the B-light-mediated inhibition of hypocotyl elongation but is positively involved in cotyledon expansion (90). The group-G bZIPs bZIP16 and bZIP68 can form homodimers or heterodimers with other group-G bZIPs (119, 120). The *Arabidopsis bzip16* mutant is hypersensitive to R light (50). In photomorphogenic growth, bZIP16 functions as a transcriptional repressor regulating genes in the light and hormone (gibberellic acid and abscisic acid) pathways (50).

2.2.4. Other transcription factors. LONG AFTER FAR-RED 1 (LAF1) is an R2R3-MYB transcription factor. The *Arabidopsis laf1* mutant has an elongated hypocotyl under FR light (4). PHYTOCHROME A SIGNAL TRANSDUCTION 1 (PAT1), a GRAS family transcription regulator, also positively regulates FR-light-mediated photomorphogenic development (9). Two other positive transcriptional regulators in the phyA-signaling pathway that were derived from ancestral transposases are FAR-RED ELONGATED HYPOCOTYL 3 (FHY3) and FAR-RED IMPAIRED RESPONSE 1 (FAR1) (52).

2.3. Light-Regulated Transcriptomic Adjustments

I have summarized dynamic chromatin remodeling and the active involvement of transcriptional regulators in responding to and transmitting light signals. The changes in nucleosome compaction and the coordinated actions of transcription factors call for massive transcriptomic adjustments in photomorphogenic seedlings.

Transcriptome profiling experiments with microarrays have revealed hundreds to thousands of genes with differential expression patterns following light treatment in wild-type *Arabidopsis* and different photomorphogenic mutants. For example, large-scale gene expression profiling has been conducted in seedlings exposed to R, FR, and B light and light/dark transitions (89). This landmark study estimated that one-third of the genome expresses differentially in response to light and that these genes belong to more than 20 cellular pathways. Consistent with the constitutive photomorphogenic phenotype, the genome-wide expression profile of the *cop1* mutant is similar to that of light-grown seedlings (88). Use of a custom-made microarray comprising 1,864 transcription factors indicated that approximately 20% of these were differentially expressed in seedlings grown in the dark or under B light (58).

The availability of commercial Affymetrix GeneChip technology has further benefited studies that use transcriptomic results to extrapolate genome-scale molecular events. Pioneering work included the identification of transcription factors as the primary responders in early FR-light responses (131), the identification of phyB and other phytochromes that together orchestrate the expression of R-light-regulated genes (130), and the successful reconstruction of phyB function in the *phyA phyB* mutant with constitutive Y276H phyB (51). Transcriptomic profiling is now routinely used to reveal molecular events at a genome-wide scale that are associated with mutations in genes related to perception or signaling in photomorphogenesis.

3. POSTTRANSCRIPTIONAL REGULATION

The genome-wide gene expression data obtained with total RNA or mRNA represent the steady-state transcript levels of annotated genes. Studies of the transcriptional activation or repression

of light-regulated genes offer only partial explanations for the light-regulated transcriptomic adjustments. In fact, the steady-state mRNA is the conclusion of multilayered events, including transcriptional activation/repression and posttranscriptional regulation such as alternative splicing and selected degradation of mRNA mediated by small regulatory RNAs. Studies of posttranscriptional regulation in photomorphogenic development are not as abundant as those of transcriptional regulation. However, the following examples indicate that posttranscriptional regulation indeed contributes to this important developmental process.

3.1. Alternative Splicing in Light Responses

Alternative splicing is a key process for enhancing proteome diversity and transcriptome plasticity without increasing the number of genes. Alternative splicing allows for the production of different mRNA isoforms from a single gene. mRNA isoforms carrying premature termination codons may undergo degradation via nonsense-mediated decay, thus reducing the accumulation of this mRNA species. Alternatively, mRNA isoforms could produce protein products with additional or missing functional domains, different protein stability, or targeting to different subcellular compartments.

In *Arabidopsis*, an estimated 40–60% of intron-containing genes may be alternatively spliced (38, 92). Nine genes, including two encoding serine/arginine-rich (SR) proteins, were found to be differentially spliced in dark- and light-grown seedlings (127). Many genes encoding important light-sensing and signaling molecules produce two or more different alternatively spliced transcripts; these include *PHYA/PHYB1* in tomato (74, 75) and *COP1* (148), *PIF6* (107), *CCA1* (38, 118), and *HYH* (126) in *Arabidopsis*. The alternatively spliced form of HYH lacks a COP1-interacting motif and thus is more resistant to selective protein degradation mediated by COP1 (126) (**Figure 3**). Transgenic plants that overexpress the gene encoding an alternatively spliced, truncated COP1 have a *cop1*-like phenotype in the dark, which implies a dominant-negative regulatory role of the truncated COP1 over the full-length protein (148). An alternatively spliced CCA1 variant, CCA1b, also functions to antagonize the full-length CCA1 by forming a nonfunctional heterodimer with CCA1a or LATE ELONGATED HYPOCOTYL (LHY) (106).

Proper alternative splicing is important for photomorphogenic development. *Arabidopsis* plants that carry mutations in a few splicing factors showed photomorphogenic defects. For example, the

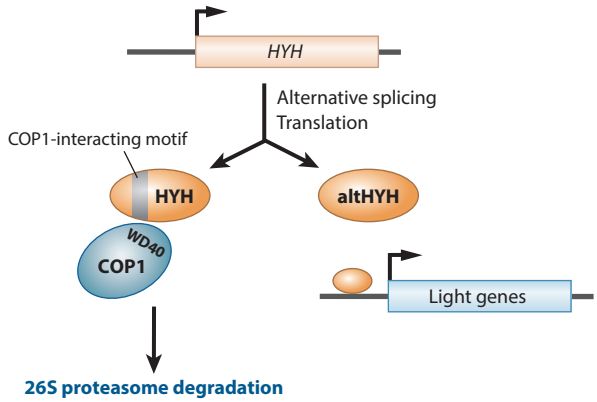


Figure 3

Increased protein stability of an alternatively spliced HYH variant (altHYH). This variant lacks a motif responsible for interaction with COP1. Increased levels of altHYH could increase the expression of light-regulated genes.

Arabidopsis skip mutant is hypersensitive to R and B light (136). SKIP is the *Arabidopsis* homolog of the mammalian Ski-interacting protein, a splicing factor and component of the spliceosome. SKIP can interact with the splicing factor SR45 to regulate pre-mRNA slicing, possibly through the recognition and cleavage of the 5′ donor and 3′ acceptor sites. The abnormal splicing of *PSEUDO-RESPONSE REGULATOR* 7 (*PRR7*) and *PRR9* mRNAs in *skip* partly explains its defects in sensing the light input signals (136). In contrast, the *Arabidopsis* mutant *reduced red-light responses in cry1cry2 background 1* (*rrc1*) is insensitive to R light (125). RRC1 is an ortholog of the human potential splicing factor SR140 and carries a C-terminal arginine/serine-rich (RS) domain. The RS domain of RRC1 is essential for RRC1 to regulate the splicing of *SR31* and *SR34a* under R light in a phyB-dependent manner (125).

The advances in high-throughput sequencing allow for the discovery of alternative splicing events in *Arabidopsis*. Although genome-wide alternative splicing in photomorphogenic *Arabidopsis* has not yet been reported, global alternative splicing regulated by light was examined in the moss *Physcomitrella patens* (139). This study showed that light triggers widespread intron retention for photosynthetic and ribosomal genes in a phyB-dependent manner.

3.2. Posttranscriptional Regulation by Small Regulatory RNAs

Small regulatory RNAs, including microRNAs (miRNAs) and small interfering RNAs (siRNAs), play a pivotal role in the posttranscriptional regulation of gene expression. *Arabidopsis* miRNAs and siRNAs can regulate the abundance and/or translation of their target mRNAs and thus play key roles in many growth and developmental stages (15, 91). Through the action of Argonaute-containing RNA-induced silencing complexes, these small RNAs function in mediating target-specific mRNA cleavage (60) and in translational repression (14, 79, 80). Phenotypic examination of *Arabidopsis* mutants carrying weak alleles of *ago1* showed a light-hypersensitive phenotype (128). This study provided genetic data to suggest that small regulatory RNAs act as negative regulators and contribute to the light-signaling pathways.

The identification of genome-wide targets of HY5 via chromatin immunoprecipitation and hybridization to an Affymetrix 1.0R tiling array revealed eight miRNA-encoding (*MIR*) genes: *MIR156d*, *MIR172b*, *MIR402*, *MIR408*, *MIR775*, *MIR858*, *MIR869*, and *MIR1888* (146). HY5 activates the expression of *MIR156d*, *MIR402*, *MIR408*, *MIR775*, and *MIR858* (146). In the *hy5* mutant, 21 selected target genes of these five *MIR*s showed high expression (146). Thus, through HY5 induction, the miRNAs could participate in repressing or at least tuning the expression amplitude of light-regulated genes (**Figure 4**).

4. TRANSLATIONAL REGULATION

Despite the quick accumulation of genome-wide gene expression data at the steady-state mRNA level, researchers have observed a moderate or even poor correlation between mRNAs and their protein products in budding yeast and mammal cells (8, 133). Much less information is available for the proteomes in photomorphogenic seedlings.

Several lines of evidence indicate that light can regulate gene expression by modulating the translation step. Dark-grown seedlings carrying a mutation in translation initiation factor 3 subunit H1 (eIF3h) showed a partial constitutive photomorphogenic phenotype (69). eIF3h is needed for the ribosome to resume scanning after translating the upstream open reading frame(s) in the 5′ untranslated regions of some transcripts (66, 112). Similar defects in skotomorphogenic development were observed in transgenic *Arabidopsis* seedlings ectopically expressing eIF3e (141). A recent study provided compelling evidence of translation control during photomorphogenesis. Paik et al.

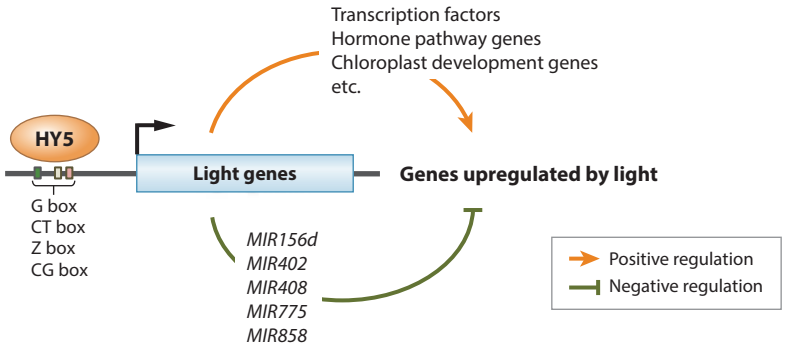


Figure 4

Activation and attenuation of photomorphogenesis by the positive regulator HY5. HY5 could activate both light-responsive genes and *MIR* genes, the latter of which encode microRNAs that function to attenuate the expression of light-responsive genes.

(103) showed that, through interaction with the cytosolic protein PENTA1, the photoreceptor phytochrome negatively regulates the translation of protochlorophyllide reductase mRNAs.

4.1. Light Increases Ribosome Occupancy on Selected Transcripts

Light can regulate the translation of photosynthetic genes. For example, the association of *ferredoxin 1* (*Fed-1*) transcripts with polysomes was enhanced by light and stabilized the *Fed-1* transcripts (32, 108). Light also triggered the translation of a photosystem I gene, *PsaD*, through polysome loading, a process that depends on the 5′ untranslated sequence of *PsaD* (124). However, the shift from low light to high light reduced the translation initiation of the light-harvesting-complex gene *Lhcbm* (95).

The technical advancements of real-time quantitative polymerase chain reaction and liquid chromatography–mass spectrometry have allowed the measurement of transcript and protein levels on a larger scale. In conjunction with fractionation of polysomes, Piques et al. (110) used these platforms to measure the transcripts and protein abundance of 35 genes from central metabolic pathways in *Arabidopsis* rosette leaves grown under diurnal changes. This study also revealed that light markedly increases the translation rate for most of the genes examined.

The combination of polysome fractionation and genome-wide transcriptome profiling enabled scientists to infer global translation in plants responding to abiotic stresses, including dehydration, elevated temperature, high salinity, oxygen deprivation, sucrose starvation, and heavy metals (12, 13, 64, 94, 98, 129). A comparison of steady-state and polysome-bound mRNAs revealed that translational enhancement has a greater impact than transcriptomic adjustment in photomorphogenic *Arabidopsis*. Liu et al. (82) showed that, during early photomorphogenesis, light increases translation efficiency by more than twofold and enhances the translation of thousands of genes. In contrast to light-enhanced translation, an unanticipated dark treatment reduced translation by 17% in *Arabidopsis*, a process that could be fully recovered by 10 min of reillumination (61).

4.2. Light Increases Ribosome Density on Selected Transcripts

For selected transcripts examined, translation enhancement could be achieved by increasing ribosome occupancy and density (82). The increase in ribosome density on transcripts might be

overlooked if polysome-mRNA populations are not further fractionated. Nonselected transcriptomic profiling of polysome-associated mRNAs offered information on the mRNA species under translation but not the regions of transcripts translated.

These concerns were recently addressed by ribosome profiling, a method combining an RNase protection assay with next-generation sequencing (53). This method could map the positions of transcripts protected by translating ribosomes at single-nucleotide resolution. Liu et al. (83) mapped the genome-wide positions of translating ribosomes in *Arabidopsis* etiolated seedlings in the dark and after light exposure. This study also revealed hundreds of *Arabidopsis* transcripts with increased or decreased ribosome density following a 4-h light treatment and showed that transcripts with increased ribosome density under light treatment preferentially encode proteins for the organization and function of chloroplasts.

4.3. Molecular Features Associated with Selected Translation by Light Signals

Genes encoding ribosomal proteins and proteins for functional chloroplasts are preferentially regulated at the translational level (82, 83), which may explain the high translation capacity and photosynthetic demands in photomorphogenesis. Other molecular features associated with transcripts preferentially translated in the light include long half-lives, short cDNA length, and transcripts with a *cis*-element (TAGGGTTT) in their 5′ untranslated region (82). This *cis*-element was confirmed to enhance translatability, although its function may not be limited to light treatment (82). In contrast, transcripts with high G+C content in their 5′ untranslated regions have low translatability in the dark (61).

Ribosome footprinting results indicated that for more than 1,500 transcripts, the upstream open reading frames initiated by ATG but not CTG will mediate translational repression of the downstream main open reading frames (83), probably to attenuate the enhanced translation efficiency by light signals (82). In contrast, miRNA-mediated translation repression is widespread but comparable between dark-grown and early photomorphogenic *Arabidopsis* seedlings (83).

These studies reveal that multiple translational mechanisms work together to orchestrate and fine-tune the light-regulated translation of diverse transcripts in *Arabidopsis* (**Figure 5**).

5. POSTTRANSLATIONAL REGULATION

Upon perceiving light, photoreceptors and key light-signaling molecules redistribute within different subcellular localizations to execute their functions (85, 134). The shuttling of these proteins into the nucleus initiates a cascade of transcriptional and posttranscriptional regulation, as summarized above. In addition to these changes in subcellular localizations, many of the translated proteins acquire their full biological functions only after they have been modified posttranslationally. Modifications including but not limited to protein phosphorylation, dephosphorylation, formation of protein complexes, and selective protein degradation play key roles in regulating the functions of photoreceptors and signaling molecules in photomorphogenic development.

5.1. Protein Phosphorylation and Dephosphorylation

Protein phosphorylation and/or dephosphorylation play key regulatory roles in gene expression and signal transduction in de-etiolating plants.

5.1.1. Phytochromes as protein kinases. An ancestral phytochrome in *Synechocystis* sp. PCC6803, Cph1, shows typical spectral reversibility with R/FR-light treatment and possesses

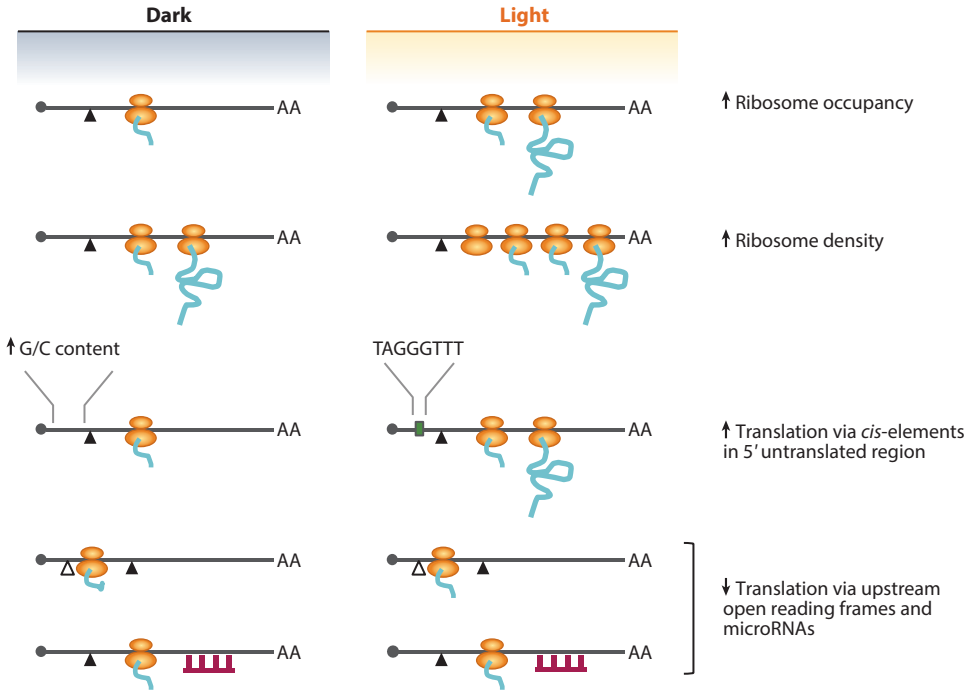


Figure 5

Translational control in photomorphogenesis. Molecular features contributing to light-enhanced translational control of mRNAs with a polyA tail (AA) include increases in ribosome occupancy and density and the presence of *cis*-elements. Features like the presence of upstream open reading frames in 5′ untranslated regions and/or the presence of microRNA target sites will inhibit the translation of mRNAs. Filled triangles indicate the translation start of the main open reading frame; open triangles indicate the translation start of the upstream open reading frame.

light-regulated histidine kinase activity (144). Cph1 and its downstream response regulator Rcp1 form a prokaryotic two-component kinase pair. The phosphorelay from Cph1 to Rcp1 is also light regulated (144). However, eukaryotic phytochromes have evolved to be serine/threonine kinases. Indeed, both algal and plant phytochromes are capable of autophosphorylation (143). The autophosphorylation of recombinant plant phytochromes is a light-regulated and intramolecular reaction, so phytochromes themselves are protein kinases (143). Several proteins were later found to be substrates of phytochrome kinase activities. These proteins include PHYTOCHROME KINASE SUBSTRATE 1 (PKS1), a negative regulator of the phytochrome-signaling pathway (37); B-light photoreceptor cryptochromes (1); auxin-responsive auxin/indole-3-acetic acid (AUX/IAA) proteins (27); and FHY1, a protein essential for the nuclear localization of phyA and the molecular responses induced by light (123).

Autophosphorylation of phytochromes also regulates the protein stability and physiological activity of the R/FR-light photoreceptor phytochromes. Lapko et al. (71) identified three autophosphorylation sites, Ser8, Ser18, and Ser599, by mass spectrometry of oat phytochrome A. Transgenic plants expressing serine-to-alanine mutations in phyA at Ser8 and Ser18 showed light hypersensitivity (71). The lack of autophosphorylation on Ser8 and Ser18 increased the protein stability of phyA and thus enhanced phyA activity in transgenic plants (71). Light hypersensitivity

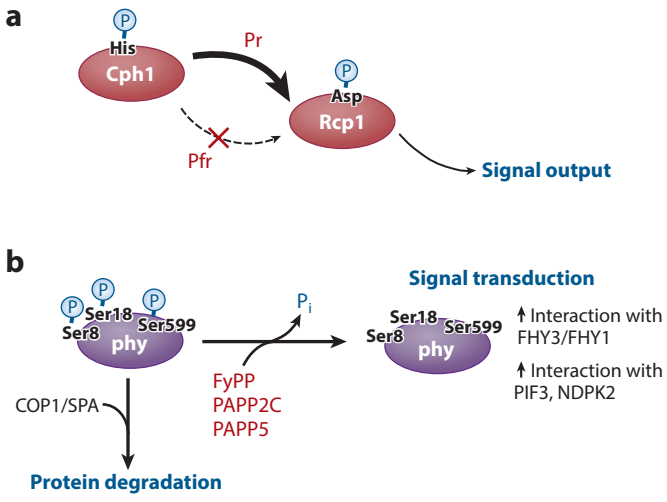


Figure 6

Posttranslational modification of the photoreceptor phytochrome. (*a*) The prokaryotic phytochrome Cph1 could autophosphorylate and transfer the phosphate to its downstream regulator Rcp1. The Pr form of Cph1 (*thick line*), but not the Pfr form, has autophosphorylation and phosphotransferase activities. (*b*) The phosphorylation or dephosphorylation of phytochrome determines its interaction with the degradation machinery (COP1/SPA) or signaling molecules (FHY3/FHY1, PIF3, NDPK2).

was also observed in transgenic *Arabidopsis* plants overexpressing oat phyA with an alanine substitution at Ser599 in the hinge region (68). The phosphorylation of Ser599 plays an inhibitory role by preventing the interaction of phytochromes with the signaling molecules, including PIF3 and NUCLEOSIDE DIPHOSPHATE KINASE 2 (NDPK2) (68).

Saijo et al. (114) reported that underphosphorylated phyA could associate with FHY3 and FHY1, which are positive regulators of phyA-signaling pathways, to execute functions under FR light. However, the binding of phosphorylated phyA with the COP1–SPA1 complex acts as a prelude for 26S proteasome-mediated degradation of phyA (see below) (114). Therefore, the phosphorylation/dephosphorylation of phyA could determine its affinity with either signaling molecules or protein degradation machinery (**Figure 6**).

5.1.2. Dephosphorylation of phytochromes by protein phosphatases. The phosphorylation status of phytochromes could be modulated by protein phosphatases. Screening of phytochrome-interacting proteins identified a cytosolic serine/threonine-specific protein phosphatase 2A, FyPP (67). FyPP can dephosphorylate autophosphorylated oat phyA, and it can dephosphorylate the Pfr form of oat phyA more effectively than it can the Pr form (67). A nucleus-localized phytochrome-associated protein phosphatase type 2C (PAPP2C) also interacts with phytochromes and mediates R-light-enhanced dephosphorylation of phytochromes (109). Moreover, a type 5 protein phosphatase (PAPP5) can preferentially interact with and dephosphorylate the Pfr form of phyA (113). PAPP5 positively regulates the light responses mediated by phytochromes, possibly dephosphorylating both N-terminal serine and the serine residue in the hinge regions. The dephosphorylation of N-terminal serine stabilizes phyA and increases its bioactivity, and that of serine in the hinge region (Ser599) enhances the interaction of phyA with NDPK2 (113), which is consistent with transgenic studies of phyA expression with serine-to-alanine mutations described above.

5.1.3. Phosphorylation of signaling molecules by casein kinase 2. Casein kinase 2 (CK2) can mediate the in vitro phosphorylation of a negative regulator of photomorphogenesis, PIF1 (16). When carrying mutations on putative phosphorylation sites (serine/threonine to alanine), PIF1 confers increased protein stability and can promote hypocotyl elongation (16). CK2 was also proposed to be the kinase responsible for phosphorylating the positive regulator HY5 (44). Unphosphorylated HY5 is more active physiologically. The phosphorylation of HY5 reduces its affinity with COP1, thus conferring more resistance to protein degradation (44). Similarly, recombinant CK2 can phosphorylate another positive regulator of photomorphogenesis, HFR1, and the phosphorylation increases the protein stability of HFR1 (105). Thus, CK2 appears to participate in the phosphorylation of both positive and negative regulators of photomorphogenesis. The phosphorylation stabilizes the positive regulators HY5 and HFR1 but promotes the degradation of the negative regulator PIF1.

5.2. Desensitizing Transcriptional Regulators via Protein–Protein Interactions

Many transcriptional regulators in the BBX, bHLH, and bZIP families are key players in photomorphogenic development. Many of these transcriptional regulators can form homodimers or heterodimers with other transcription factors. The combined interactions among both positive and negative transcriptional regulators offer an opportunity for fine-tuning the light-regulated transcriptional activities.

Increasing evidence suggests that bHLHs possess diverse functions through the formation of homodimers as well as heterodimers. A few atypical bHLHs lacking DNA-binding domains function to attenuate the transcriptional activities of PIFs. For example, PHYTOCHROME RAPIDLY REGULATED 1 (PAR1) forms a heterodimer with PIF4 and reduces the DNA-binding activity of PIF4 (43). Under shade conditions, HFR1 forms heterodimers with PIF4 and PIF5 to form a non-DNA-binding complex, thus preventing PIF4/PIF5 from triggering the expression of cell-elongation genes (49). This competitive inhibition could be compromised by the formation of a heterodimer between KIDARI (KDR), another atypical bHLH, and HFR1 (48), which indicates a double-negative regulation of PIF activities.

The light-regulated phyA nuclear accumulation requires FHY1 and its homolog FHY1-LIKE (FHL) (40, 46). FHY3/FAR1 can activate the expression of FHY1 and FHL. However, this activation can be attenuated by the binding of HY5 to FHY3/FAR1 and to the ACGT-containing element in the promoters of *FHY1* and *FHL* (78).

The attenuation of transcriptional activity is not limited to interactions between transcriptional regulators. Park et al. (104) reported that the Pfr form of phyB can interact with PIF1 and PIF3. This binding sequesters PIF1 and PIF3 from binding to their target promoters.

5.3. Selective Protein Degradation

Selective protein degradation is a key regulatory step in photomorphogenic development (**Figure 7**). Many photoreceptors and signaling molecules undergo posttranslational regulation by light. Genetic screening of *Arabidopsis* mutants with aberrant photomorphogenesis phenotypes has revealed many components in the ubiquitin/26S proteasome pathway. The most well-studied group includes the COP1–SUPPRESSOR OF PHYA-105 (SPA) complex, the COP9 signalosome (CSN), and the COP10–DET1–DDB1 (CDD) complex (73). Genetic screening has also identified EID1, an F-box protein functioning in the phyA pathway (33, 93). The F-box proteins ATTENUATED FAR-RED RESPONSE (AFR) (45) and MORE AXILLARY BRANCHES

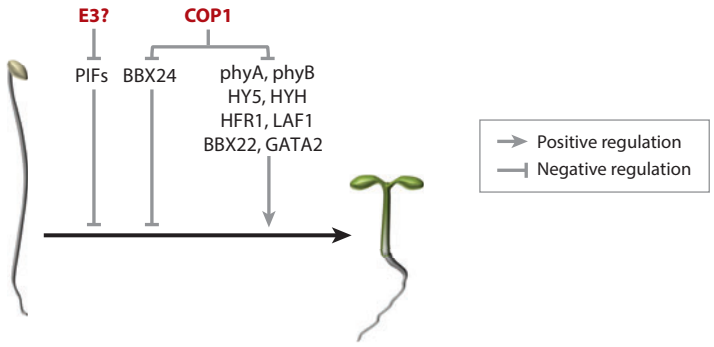


Figure 7

Selective protein degradation of transcriptional regulators in photomorphogenic development. COP1 mediates the degradation of both positive and negative regulators in photomorphogenesis. E3 ligases responsible for the degradation of PIFs remain unknown.

2/ORESARA 9 (MAX2/ORE9) (121) were also identified as positive regulators in the phyA- and light-signaling pathways, respectively.

5.3.1. Selective degradation of photoreceptors. The protein abundance of photoreceptors can be regulated posttranslationally by degradation. COP1 can interact with phyA and mediate the ubiquitination and degradation of phyA (116). Light triggers the translocation of phyB into the nucleus, where phyB is ubiquitinated by COP1 for degradation (55). PIFs can enhance the COP1-mediated degradation of phyB (55), which is consistent with their negative functions in light responses.

5.3.2. Selective degradation of positive regulators. Multiple transcriptional regulators positively regulating photomorphogenesis are degraded in the dark via the 26S proteasome in a COP1-dependent manner. These regulators include HY5 (101), HYH (47), BBX22/LZF1 (19), and a GATA transcription factor, GATA2 (87). The degradation of these positive regulators prevents them from triggering photomorphogenic development in the dark, thus ensuring proper skotomorphogenesis. Under FR light, COP1 also mediates the degradation of positive regulators such as HFR1 (56) and LAF1 (117) for degradation as a means to attenuate the phyA signaling.

Light-induced translocation of COP1 from the nucleus to the cytosol (135) releases positive regulators to turn on genes upregulated by light. Under B light, cry1 could interact with SPA1, thus suppressing the function of COP1, because SPA1 is needed for the E3 ligase activity for the COP1–SPA complex (81).

5.3.3. Selective degradation of negative regulators. The light-triggered degradation of negative regulators relieves their roles in activating genes for skotomorphogenesis, which include genes involved in cell elongation. PIFs are the most well-characterized negative transcriptional regulators of photomorphogenesis. In light, PIF3 is phosphorylated in a phyA- and phyB-dependent manner. This phosphorylation is followed by the localization of PIF3 in nuclear speckles and then quick degradation (2). Light also regulates the 26S proteasome–mediated degradation of PIF1 and PIF5 (17, 122). The E3s responsible for the degradation of PIFs remain to be identified. In contrast, COP1 could interact with the negative regulator of photomorphogenesis BBX24/STO (47). BBX24 only transiently accumulates in seedlings exposed to light signals, and this light-regulated degradation depends on interaction with COP1 (142).

6. CONCLUDING REMARKS

The regulation of gene expression could occur at different levels in the central dogma of molecular biology. As highlighted here, environmental light signals set off a series of molecular actions at almost every step of the dogma for gene expression regulation.

Light upregulates the expression of genes by triggering the translocation of photoreceptors from the cytosol to the nucleus and negative regulators such as COP1 from the nucleus to the cytosol, relaxing the chromatin structure through histone modification, activation of transcriptional cascades by positive transcription factors, and massive enhancement of translation. The derepression of photomorphogenic development could also be achieved by inactivating negative regulators through the formation of nonproductive protein complexes, phosphorylation, and degradation.

Clearly, most or all of these molecular actions should be properly inhibited when seedlings are grown in the dark. Even with growth in the light, light signals need to be properly attenuated to avoid exaggerated light responses. The attenuation or desensitization mechanisms include the sequestering of photoreceptors and positive regulators in the cytosol, formation of a more compacted chromatin structure, repression of gene expression by negative regulators, production of miRNAs, and phosphorylation and degradation of photoreceptors.

Genes contributing to photomorphogenesis could be regulated at one or more levels in the central dogma. Gaining a comprehensive and mechanistic understanding of photomorphogenesis will demand continued efforts in dissecting individual genes and genome-wide surveys of gene expression at all levels.

FUTURE ISSUES

1. How are light-regulated transcriptional complexes formed and regulated?
2. Is there coordinated regulation among chromatin structure, transcription, and alternative splicing during photomorphogenesis?
3. Are the alternatively spliced variants nonproductive, or do they contribute to the increase of proteome complexity?
4. Genome-wide profiling is needed of both mRNAs and small regulatory RNAs for the discovery of microRNA–mRNA pairs that function to fine-tune the *Arabidopsis* transcriptome.
5. Further work is needed to uncover key regulators and/or regulatory mechanisms that determine the widespread translation enhancement in response to light treatment, especially for mRNAs with comparable abundance before and after light exposure.
6. Additional E3 ligases responsible for selective degradation of signaling molecules in photomorphogenesis should be explored, especially the time-dependent degradation of negative and positive regulators.
7. Phosphoproteome mapping during photomorphogenesis should be carried out, then followed by mechanistic studies to determine the biological impact of protein phosphorylation/dephosphorylation.

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