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Update on Development

The Role of the *COP/DET/FUS* Genes in Light Control of Arabidopsis Seedling Development[1]

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Light is vital to plant life, not only as an energy source for photosynthesis but also as an important environmental signal regulating development and growth. Light affects almost every stage of plant development (Kendrick and Kronenberg, 1994), including seedling development, which represents one of the most dramatic and best characterized processes (von Arnim and Deng, 1996). In *Arabidopsis thaliana*, for example, the morphology of the embryo in the imbibing seed (d 1), as well as the emerging seedling from the seed coat (d 2), are minimally affected by light conditions (Wei et al., 1994b). Soon after, however, seedling morphogenesis differs drastically, depending on the light environment (Fig. 1). Light-grown seedlings exhibit short hypocotyls and open and expanded cotyledons. Cell-type differentiation and chloroplast development are soon established, and photosynthetically related genes are highly expressed. The shoot apical meristem is activated to produce true leaves and the plants proceed with further vegetative and reproductive growth soon thereafter. This development pattern in light is known as photomorphogenesis. In contrast, when seedlings are grown in complete darkness, they undergo a developmental program known as skotomorphogenesis or etiolation, in which the cotyledons remain folded and undeveloped, while the hypocotyls rapidly elongate. The apical hook serves to protect cotyledons and the quiescent shoot meristems as the seedling elongates rapidly to reach for the light. Instead of developing chloroplasts, the cotyledon cells form etioplasts that can readily convert into chloroplasts when exposed to light. This process is known as greening or de-etiolation. In addition, etiolated seedlings display a very different gene expression pattern from that determined by light. After the initial elongating growth, the seedlings come to a developmental arrest in the continuous absence of light.

In higher plants, light-controlled physiological and developmental responses are mediated through at least three families of photoreceptors: phytochromes, cryptochromes, or blue-light receptors, and UV-B receptors, depending on the wavelengths of light to which they are most sensitive. In Arabidopsis, genes for five phytochromes, phytochrome A, B, C, D, and E, and a blue-light receptor, CRY1 (or HY4), have been isolated. Recent reviews of the photobiology and molecular biology of photoreceptor action have been published (Furuya 1993; Vierstra, 1993; Quail, 1994; McNellis and Deng, 1995; Quail et al., 1995; Chamovitz and Deng, 1996). In this *Update* we will emphasize the role of a group of negative regulators genetically identified as constitutive photomorphogenic (*COP*) or de-etiolated (*DET*) loci.

A TENTATIVE CLASSIFICATION OF THE *COP/DET* MUTANTS

Genetic screens have been fruitful in identifying regulatory components involved in light-controlled seedling development. Based on contrasting light- and dark-grown seedling morphology, two types of loss-of-function mutants were recovered. Mutations in positive regulators of photomorphogenesis result in a *hy* (hypocotyl elongated) phenotype, a partial etiolated morphology under defined light conditions, whereas mutations in the negative regulators result in a *cop* or *det* phenotype when grown in the dark. The *hy* mutants include mutants of photoreceptors as well as downstream signaling components such as *hy5* (Koornneef et al., 1980), *fhy1*, and *fhy3* (Whitelam et al., 1993).

The *cop/det*-type mutants can be further classified into three general groups (Table I). Mutants in the first group have so far been identified in several Arabidopsis loci (*cop1*, *det1*, and *cop8-15*) (Chory et al., 1989; Deng et al., 1991; Wei and Deng, 1992; Wei et al., 1994b; Miséra et al., 1994; Kwok et al., 1996). These mutants exhibit a light-independent pleiotropic phenotype: dark-grown seedlings resemble their light-grown siblings in overall morphology, cell and plastid differentiation, and expression pattern of light-regulated genes. This group of mutants will be the focus of this review.

The second group of mutants have opened cotyledons without apical hooks but display normal etioplast development and elongated hypocotyls when grown in the dark (*cop2/amp1*, *cop3/hls1*, and *cop4*) (Chaudhury et al., 1993; Hou et al., 1993; Lehman et al., 1996). Whereas *cop2* and *cop3* do not significantly affect light-regulated gene expression, *cop4* shows moderate de-repression of nuclear-encoded light-induced gene expression (*CAB1*, chlorophyll *a/b*-binding protein) in the dark (Hou et al., 1993).

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Table I. *Summary of negative regulatory loci of photomorphogenesis in Arabidopsis*

COP/DET Gene	Other Names	Dark-Grown Mutant Seedling Morphology	Lethality of Null Mutant	Refs.
COP1	*FUS1, EMB168*	Pleiotropic	Yes	Deng et al., 1991
COP8	*FUS8, EMB134*	Pleiotropic	Yes	Wei et al., 1994
COP9	*FUS7, EMB143*	Pleiotropic	Yes	Wei and Deng, 1992
COP10	*FUS9, EMB144*	Pleiotropic	Yes	Wei et al., 1994
COP11	*FUS6, EMB73*	Pleiotropic	Yes	Wei et al., 1994; Castle and Meinke, 1994
COP12	*FUS12*	Pleiotropic	Yes	Miséra et al., 1994; Kwok et al., 1996
COP13	*FUS11*	Pleiotropic	Yes	Miséra et al., 1994; Kwok et al., 1996
COP14	*FUS4*	Pleiotropic	Yes	Miséra et al., 1994; Kwok et al., 1996
COP15	*FUS5*	Pleiotropic	Yes	Miséra et al., 1994; Kwok et al., 1996
DET1	*FUS2*	Pleiotropic	Yes	Chory et al., 1989
COP2	*AMP1, PT1*	Open cotyledons	No	Hou et al., 1993; Lehman et al., 1996; Chaudhury et al., 1993
COP3	*HLS1*	Open cotyledons	No	Hou et al., 1993; Lehman et al., 1996
COP4		Open cotyledons	Unknown	Hou et al., 1993; Lehman et al., 1996
DET2	*COP7*	Short hypocotyl	No	Chory et al., 1991
DET3		Short hypocotyl	Unknown	Cabrera y Poch et al., 1993
PRC1		Short hypocotyl	Unknown	Desnos et al., 1996
DIM		Short hypocotyl	Unknown	Takahashi et al., 1995
CPD		Short hypocotyl	No	Szekeres et al., 1996

The primary seedling phenotype of the third group is a short hypocotyl when grown in darkness for less than 5 d (*det2, det3, dim, prc1, cpd*) (Chory et al., 1991; Cabrera y Poch et al., 1993; Takahashi et al., 1995; Desnos et al., 1996; Szekeres et al., 1996). Significant cotyledon expansion and opening also occurred after extended dark growth (more than 1 week) in most of those mutants (except *prc1*), although no sign of chloroplast development was observed. In addition, true leaves can initiate and develop after extended growth in the dark. The short-hypocotyl phenotype for the *prc1* mutant is specifically associated with the dark-grown seedling, since the hypocotyl growth of the light-grown mutant is still under normal light control. This indicates that the mechanism underlying hypocotyl elongation in the dark is different from that in the light (Desnos et al., 1996).

Unlike the first group of mutants, the second and third groups of mutants exhibit partial light-dependent seedling development in darkness. Since many other factors also affect different aspects of seedling morphogenesis, such as hormones, nutrients, and metabolites, it is likely that some loci in these two groups may define regulatory components directly related to those signaling pathways. For example, *cop3* has turned out to be allelic to *hookless1* (*hls1*) (Lehman et al., 1996), which was identified based on ethylene responsiveness, and *amp1* (allelic to *cop2*) was isolated based on altered cytokinin responsiveness (Chaudhury et al., 1993). *cop4* lacks a normal gravitropic response (Hou et al., 1993); therefore, COP4 may also be involved in gravity response. More recently, it has been shown that *DET2* and *CPD* (CYP90) encode enzymes in the biosynthetic pathway of brassinosteroids (Li et al., 1996; Szekeres et al., 1996); thus, the light regulatory network may be interlinked with other signaling pathways and light might exert its effect on an aspect of seedling morphology through the action of hormones or other factors. Therefore, some of these less pleiotropic loci may represent components of the "cross-talk" between the light regulatory network and other signaling pathways.

THE PLEIOTROPIC *COP/DET* LOCI ARE ALSO DEFINED BY THE *FUSCA* MUTATIONS

A phenotype common to all severe alleles of the first group of *cop/det* mutants is the accumulation of purple pigment (anthocyanin) in the mature seed and young seedlings, a feature that was used for screening *fusca* mutants (Müller, 1963; Castle and Meinke, 1994; Miséra et al., 1994). Detailed characterization of 12 available *fusca* loci suggested that 10 of them show pleiotropic photomorphogenic development in the dark (Miséra et al., 1994; Kwok et al., 1996), among which 6 are allelic to the pleiotropic *COP/DET* loci (*COP1, DET1, COP8-11*) mentioned above and 4 define novel loci (Kwok et al., 1996). Thus, a total of 10 pleiotropic *COP/DET/FUS* loci have been identified.

When grown in darkness, the *cop/det/fus* mutants exhibit almost all aspects of the phenotype normally observed in light-grown seedlings (Fig. 1). The dark-grown mutants exhibit short hypocotyls and open cotyledons without apical hooks. Cotyledon cell enlargement and differentiation resemble those of wild-type, light-grown plants. Likewise, instead of etioplasts, the plastids develop into an intermediate form that looks like it is on its way to becoming a chloroplast. Tissue-specific plastid differentiation is also affected, since greening and chloroplast development have also been observed in mutant roots under light conditions. This is also accompanied by ectopic expression of photosynthesis-related genes in roots and the chalcone synthase gene in mesophyll cells of leaves (Chory and Peto, 1990). Moreover, the pattern of gene expression is similar to that of light-grown siblings. Both nuclear- and chloroplast-encoded photosynthesis-related genes are de-repressed in the dark and in dark-adapted plants. This pleiotropic phenotype implies that the light switch controlling photomorphogenic and skotomorphogenic programs is no longer functional in these mutants, resulting in a constitutive default photomorphogenic developmental pathway (McNellis and Deng, 1995).

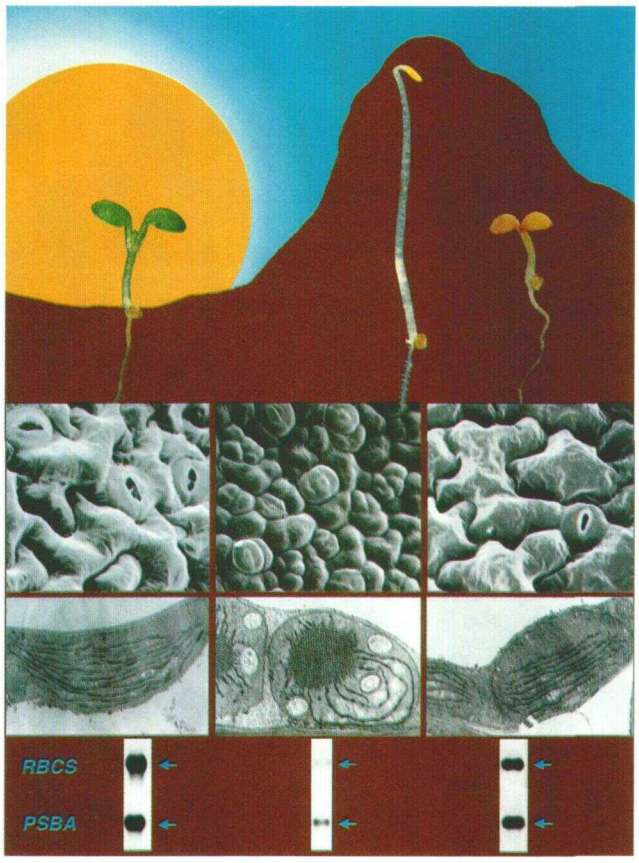

Figure 1. Comparison of the phenotypic characters of a representative pleiotropic *cop* mutant with wild-type seedlings. The light-grown wild-type seedling (left), dark-grown wild-type seedling (middle), and a typical dark-grown pleiotropic *cop* mutant seedling (right) are shown at the top. The panels below illustrate the characteristics of the cotyledon surface cell morphology, plastid morphology, and expression patterns of two selected nuclear-encoded (*RBCS*) and plastid-encoded (*PSBA*) genes of the corresponding seedlings on the top.

THE *COP/DET/FUS* GENES ARE ESSENTIAL FOR REPRESSION OF PHOTOMORPHOGENIC DEVELOPMENT IN DARKNESS

The recessive nature of these pleiotropic *cop/det/fus* mutations is consistent with their wild-type gene products acting to repress photomorphogenesis in the dark and light signals releasing such repressive activity. Although this genetic model is only one way of interpreting the mutant phenotype, it has gained support from additional molecular and genetic studies. Transgenic Arabidopsis seedlings overaccumulating COP1 show a partially etiolated phenotype: longer hypocotyl under dark/light-cycled white light as well as continuous far-red or blue-light conditions, demonstrating the suppressor activity of COP1 on photomorphogenic development (McNellis et al., 1994b). Genetic analysis of double mutants between the pleiotropic *cop/det/fus* mutations and the photoreceptor mutations suggested that these gene products act downstream of photoreceptors (Fig. 2; Chory et al., 1989; Deng et al., 1991; Wei and Deng, 1992; Miséra et al., 1994; Wei et al., 1994b; Kwok et al., 1996).

Within the context of this genetic model, it is not surprising that all severe mutations also lead to a *fusca* phenotype, since anthocyanin accumulation is one of the light-inducible traits that increases quantitatively with higher light intensity. Therefore, a complete loss of function of these repressive components would mimic the action of the highest light intensity extreme, under which condition increased anthocyanin accumulation would be expected. In addition, some other characteristics of the photomorphogenic *fusca*, such as very short hypocotyl and severe growth retardation, resemble those of highly photostressed seedlings. The lethality of *fusca* mutant alleles after the seedling stage may result from the accumulated stress and/or may indicate that, in addition to their function as repressors of photomorphogenesis in darkness, the *COP/DET/FUS* loci are essential for adult plant development in the light.

Whereas the pleiotropic *COP/DET/FUS* loci may be involved also in other regulatory processes, several lines of evidence support the conclusion that they are specifically involved in the light control of development and that they represent integral parts of the light regulatory network. First, weak mutations in *cop1* and *det1* loci produce rather specific and striking defects in light responses while allowing for the completion of the life cycle. Second, the only detectable phenotype of seedlings overexpressing COP1 is a partial etiolated response under specific light conditions (McNellis et al., 1994b). The third and most recent research shows that overexpression of a COP1 N-terminal 282-amino acid fragment (N282) results in a dominant negative effect specifically associated with the photomorphogenic development of the seedlings (McNellis et al., 1996). This includes chloroplast-like plastid development and activation of normally light-induced genes in the dark, whereas the effect on the expression of stress- and pathogen-inducible genes is minimal.

FUNCTIONAL RELATIONSHIP OF THE PLEIOTROPIC *COP/DET/FUS* GENES

Two general hypotheses have been proposed to explain the nearly identical phenotypes in all 10 pleiotropic *cop/det/fus* mutants (Castle and Meinke, 1994; Miséra et al., 1994; McNellis and Deng, 1995). One hypothesis is that each of the genes acts in parallel pathways and is independently required to repress photomorphogenic development, and the other hypothesis is that these genes work in proximity to each other in the same regulatory pathway. Recently, several lines of evidence supporting the latter hypothesis have been reported, as described below.

Genetically, synthetic lethality and phenotype enhancement between two weak and viable alleles of *cop1* and *det1* loci have been observed (Ang and Deng, 1994), implying that the two loci act in the same pathway. Biochemical characterization of COP9 indicated that it exists in a complexed form (Wei et al., 1994b). In addition, the COP9 complex does not accumulate in *cop8* and *cop11* mutants, which suggests that both COP8 and COP11 are required for the formation or the stability of the complex. This observation demonstrates that at least the three genes, *COP8*,

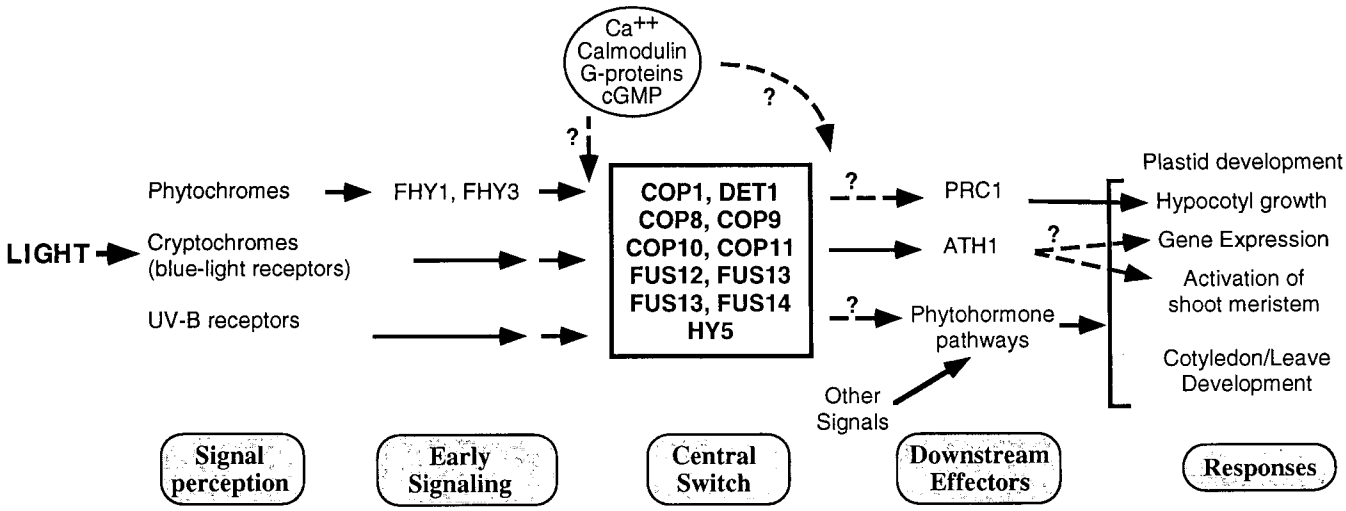

Figure 2. Diagram of hypothetical light-signaling cascade during seedling development in Arabidopsis. Light is perceived by three families of photoreceptors: phytochromes, cryptochromes, and UV-B receptors. The signals are transmitted through receptor-specific early-signaling components such as FHY1 and FHY3 (phytochrome A-specific) and eventually merge to the central switch as represented by 10 COP/DET/FUS products and HY5. The central processor then brings about the light responses through interaction with putative response-specific effectors such as PRC1 and ATH1. It may also cross-talk with phytohormone pathways to convey its effect in some responses. It should be emphasized that phytohormones are able to influence overlapping biological processes during seedling development independently of light signals. The relative position of signaling molecules including Ca^{2+}, calmodulin, G proteins, and cGMP are undetermined in this model. The arrows denote the flow of information and do not indicate positive or negative interactions in genetic terms. Question marks and dashed arrows indicate speculative paths with no experimental evidence either positive or negative.

COP9, and *COP11*, act in the same pathway. Last, the COP9 complex has been shown to play a role in nuclear import or nuclear retention of GUSCOP1 (Chamovitz et al., 1996), connecting COP1 with the COP9 complex in the same pathway.

SOME OF THE PLEIOTROPIC *COP/DET/FUS* GENES ARE DEFINED AS A MULTISUBUNIT NUCLEAR COMPLEX

Two approaches have independently provided definitive evidence that multiple pleiotropic *COP/DET/FUS* genes encode subunits of the COP9 complex. Using antibodies raised against COP11 (also called FUS6, Castle and Meinke, 1994), Staub et al. (1996) found that COP9 and COP11 co-fractionated in the same large size fractions (560 kD) and co-immunoprecipitated each other from total plant extract. Furthermore, biochemical purification of the COP9 complex from cauliflower, a close relative of Arabidopsis (Chamovitz et al., 1996), revealed that the complex is spherical, about 12 nm in diameter, and contains 12 subunits with equal molar amounts. Direct amino acid sequencing of the individual proteins in the complex not only confirmed the identity of the expected COP9 subunit but also revealed that the COP11 is also a subunit in the purified complex. Together with the above biochemical observation in Arabidopsis, co-purification of COP11 with COP9 from cauliflower provides the best proof that multiple pleiotropic *COP/DET/FUS* genes encode subunits of the same complex. It will be interesting to determine the identities of other subunits of the COP9 complex and to see whether they correspond to any pleiotropic *COP/DET/FUS* genes. Although immunoblot analysis with COP1 antibodies indicates that COP1 is not part of the purified COP9 complex, it remains to be addressed whether COP1 and others could be part of the larger, light-labile version of the "dark" COP9 complex, which was observed in the dark-grown Arabidopsis seedlings (Wei et al., 1994b).

Both immunostaining with the COP9 antibodies and histochemical staining of GUS-COP9 fusion protein suggest that COP9 is nuclear localized in both Arabidopsis and cauliflower (Chamovitz et al., 1996; Staub et al., 1996). Since COP9 exists only in the complexed form (Wei et al., 1994a), the COP9 complex must be nuclear. It is interesting to note that, despite its lack of recognizable nuclear localization signals, GUS-COP9 can be correctly localized into nuclei of root cells of transgenic plants. Therefore, it is possible that partial or full assembly of the COP9 complex, which would recruit other subunit(s) containing nuclear localization signals, may be prerequired for its nuclear translocation. Consistent with this possibility, it has been observed that, whereas GUS-COP9 displays a nuclear staining in roots of *cop1*, *det1*, *cop9*, and *cop10* mutants, it is cytoplasmic in *cop8* and *cop11* (Chamovitz et al., 1996), both of which probably represent mutations in genes encoding subunits of the COP9 complex.

HOW DOES LIGHT REGULATE *COP/DET/FUS* ACTIVITY?

The genetic model predicts that when light signals are perceived by photoreceptors they are transduced to abro-

gate the suppressive activities of the COP/DET/FUS products over photomorphogenic development. Recent cloning of four of these genes, COP1 (Deng et al., 1992), FUS6/COP11 (Castle and Meinke, 1994), DET1 (Pepper et al., 1994), and COP9 (Wei et al., 1994a), provide tools for molecular analysis of this light-inactivation mechanism. Analysis of the expression levels of those gene products showed that protein accumulation of COP1, COP9, and COP11 and the mRNA level of DET1 are not subject to light regulation and are ubiquitously present in most, if not all, tissue types (McNellis et al., 1994a; Pepper et al., 1994; Wei et al., 1994a; Staub et al., 1996). Therefore, light likely modulates their activities post-translationally through protein-protein interaction, protein modification, subcellular localization, or a combination of these processes.

Aside from the COP9 complex (both COP9 and COP11), examination of the subcellular localization of fusion proteins between GUS reporter and COP1 or DET1 suggested that they are also nuclear regulators (Pepper et al., 1994; von Arnim and Deng, 1994). Whereas the nuclear location of the COP9 complex and DET1 seems to be independent of light conditions, the nucleocytoplasmic partitioning of COP1 is regulated by light in a cell-type-dependent manner (von Arnim and Deng, 1994; Fig. 3). In hypocotyl cells of stably transformed Arabidopsis seedlings and epidermal cells of onion bulb, the GUS-COP1 protein is enriched in the nucleus in darkness and is excluded from the nucleus under constant white light. When a dark-grown seedling is exposed to light, the protein slowly repartitions from a nuclear to a cytoplasmic location and vice versa for a light-grown seedling transferred into darkness. Moreover, the nuclear GUS-COP1 level appears to correlate quantitatively with the extent of suppression of photomorphogenic development in hypocotyl cells. In root cells, however, GUS-COP1 is constitutively nuclear, which is consistent with the established role of COP1 in suppressing root chloroplast development in both light and darkness. Therefore, it is hypothesized that COP1 acts inside the nucleus to repress photomorphogenesis and that light modulation of COP1 activity involves a tissue-type-specific nucleocytoplasmic repartitioning (Fig. 3). Since the transgene encoding the GUS-COP1 fusion protein can completely rescue a null mutant of *cop1* and thus is functional (A.G. von Arnim and X.-W. Deng, unpublished data), the localization pattern of GUS-COP1 is likely to be biologically relevant.

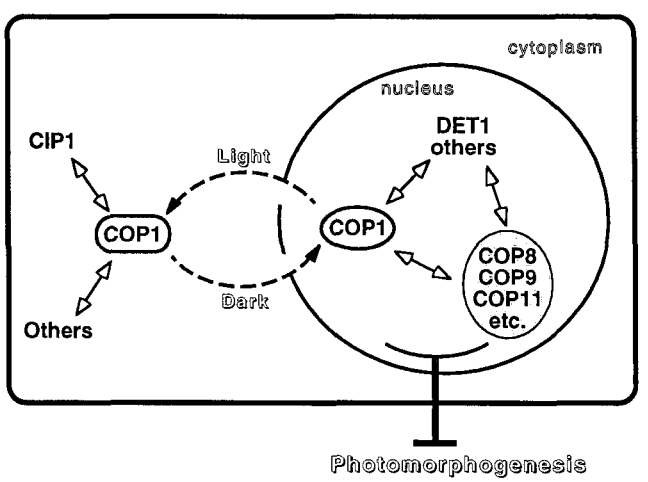

Figure 3. Hypothetical model illustrating the relationship of the pleiotropic *COP/DET/FUS* gene products. All of the gene products are proposed to act within the nucleus and together lead to repression of photomorphogenic seedling development. Light signals disrupt those nuclear interactions, their ability to repress photomorphogenesis, and a concomitant repartitioning of COP1 between the nucleus and cytosol. Note that the dashed arrows between the COP1 in nuclear and cytosolic compartments indicate the direction of concentration change and not necessarily the direction of movement of the COP1 itself.

The light control over GUS-COP1 nucleocytoplasmic partitioning has the following implications: First, COP1 exclusion from the nucleus under light may represent a mechanism for disabling COP1's suppressive function in photomorphogenesis. In the dark COP1 acts as a nuclear regulator, which likely turns off the photomorphogenic program by interacting with some yet unknown targets. By reducing its abundance in the nucleus, light makes COP1 less effective in interacting with its intended targets; thus, it becomes less able to suppress photomorphogenic development. By regulating the relative nuclear abundance of COP1, this mechanism could easily achieve a quantitative suppression of photomorphogenic development under different intensities of light. Furthermore, this model also provides a framework for examining the functional role of other pleiotropic *COP/DET/FUS* genes (Fig. 2). For example, GUS-COP1 was unable to localize to nuclei of dark-grown hypocotyl cells in those pleiotropic *cop* mutants defective in the COP9 complex (Chamovitz et al., 1996). This observation suggests that the COP9 complex is involved in COP1 nuclear translocation or nuclear retention in darkness. This role of the COP9 complex would be consistent with the phenotype of their mutations.

The slow kinetics of the GUS-COP1 nuclear localization during a light-dark transition (von Arnim and Deng, 1994) would imply that its changed nuclear abundance is unlikely to be the primary cause of the initial development switch, but more likely it is a way of maintaining COP1 in an inactive state. It is possible that when a dark-grown seedling is exposed to light COP1 may be initially transiently inactivated by a still unknown mechanism. Subsequent exclusion of COP1 from the nucleus would serve as an efficient way to prevent its suppressive action on photomorphogenic development under constant light. Meanwhile, the COP1-interactive protein CIP1 (Matsui et al., 1995), which displays a cytoskeleton-type cellular distribution pattern, has the potential to be involved as a cytoplasmic anchor protein in regulating access of COP1 to the nucleus through protein-protein interactions.

IMPLICATIONS FOR MULTIPLE FUNCTIONAL MODULES IN COP1

The central role of *COP1* as a light-inactivatible repressor of photomorphogenesis warrants some discussion about the structural features of its encoded protein. Whereas *COP9*, *DET1*, and *FUS6/COP11* encode novel proteins that

have no obviously identifiable homology to other known proteins or motifs, COP1 has a novel combination of the following recognizable motifs: a ring-finger zinc-binding domain at the amino-terminal region, followed by a coiled-coil helix structure, and several WD-40 repeats at the carboxyl-terminal (Deng et al., 1992; McNellis et al., 1994a). The coiled-coil and WD-40 repeats are likely surfaces for mediating protein-protein interactions, whereas the zinc finger domain has the potential to interact with either or both proteins and nucleic acids. The multiple interactive motifs of COP1 provide a physical basis for its being a central player in interacting with multiple upstream and downstream components in the light regulatory cascades. Examination of the available ethyl methanesulfonate-induced recessive *cop1* alleles (McNellis et al., 1994a) revealed that subtle changes in the WD-40 repeat regions of COP1 protein lead to a severe phenotype similar to complete loss-of-function mutations. However, the *cop1-4* mutation, which results in a COP1 protein with only the 282 N-terminal amino acids (N282) at about 10% of wild-type level and a complete removal of the WD-40 domain, produces one of the weakest phenotypic defects. This indicates that the N282 protein itself retains significant activity, whereas imperfections in the WD-40 repeat regions are detrimental to this function. Consistent with this idea, when the N282 portion of COP1 is expressed in transgenic seedlings, it produced a dominant negative phenotype that is partially de-etiolated in the dark, with hypocotyl elongation that is hypersensitive to light inhibition (McNellis et al., 1996). The ability of the N282 protein to mask endogenous COP1 function could be interpreted to mean that N282 itself may contain the modules responsible for interacting with downstream targets of COP1 and that the phenotype results from depletion of COP1 downstream targets due to the presence of high levels of N282.

CANDIDATES FOR DOWNSTREAM EFFECTORS OF COP/DET/FUS PROTEINS

As nuclear regulators, any COP/DET/FUS protein has the potential to directly affect the expression pattern of genes responsible for photomorphogenesis or skotomorphogenesis. This can be achieved in a variety of ways. For example, a given COP/DET/FUS protein or complex can modulate the expression pattern of light-regulated genes by directly interacting with the light-responsive promoters, or specific transcription factors, which bind to light-responsive promoters, or by regulating the expression of genes encoding the transcription factors. These possibilities can be investigated by identifying either direct protein-protein interactive partners (Matsui et al., 1995) or their potential DNA-binding sites. Although no conclusive evidence for either of the possibilities has been provided yet, several transcription factors whose expression is regulated by light could represent potential candidates.

One appealing candidate is *ATH1*, which encodes a homeodomain protein whose expression is transiently induced by light in Arabidopsis seedlings (Quaedvlieg et al., 1995; Fig. 2). However, unlike many photosynthesis-related genes such as *CAB* (chlorophyll *a/b*-binding protein), *ATH1* gene expression is independent of chloroplast development and the light induction is transient. It is interesting that mutations in *cop1* and *det1* disrupt its light-dependent expression, resulting in the accumulation of *ATH1* mRNA in the dark. Many proteins with homeodomains are known as transcriptional regulators, capable of controlling developmental patterns through modulating meristematic cell division activities at the site of primordia formation (Hake et al., 1995). Accordingly, the *ATH1* gene contains a Pro-rich region and two Ser/Thr-rich regions that could function as transcriptional activation domains (Quaedvlieg et al., 1995). Therefore, it is possible that *ATH1* could be one of the downstream targets of COP/DET/FUS proteins, which, when induced in the light, activates a chloroplast-independent morphogenic program such as cell division in shoot meristems. Similarly, the expression of Arabidopsis *ATHB-2* and *ATHB-4*, both of which encode proteins containing homeodomains and Leu zipper motifs, are strongly induced by far-red-rich light treatment (Carabelli et al., 1993, 1996). However, it has not been reported whether *cop/det/fus* mutations affect the gene expression of *ATHB-2* and *ATHB-4*.

Since photomorphogenesis is a complex process involving many cell-type-specific and organ-specific morphogenic responses, the pleiotropic *COP/DET/FUS* products probably have multiple downstream effectors. For example, COP/DET/FUS may transduce light signals and influence an aspect of morphogenic development by interacting with phytohormone pathways and/or other regulatory pathways. In fact, some of the negative regulators listed in the second and third groups in Table I may represent those downstream effectors controlling specific aspects of the morphogenic responses. The recent findings by Szekeres et al. (1996) and Li et al. (1996) that DET2 and CPD are involved in the brassinosteroid biosynthetic pathway and that application of brassinolide can partially compensate the hypocotyl phenotype of most *cop/det/fus* mutants in an allele-specific manner would be consistent with this speculation. However, it is also possible that light and brassinosteroids independently affect hypocotyl growth during seedling development. To distinguish between these hypotheses, it is necessary to address whether light affects the cellular level (production/degradation), perception, and signal transduction of brassinosteroids, or whether photomorphogenic *cop/det/fusca* mutants have a lower than normal level of these molecules.

COP/DET/FUS MAY REPRESENT A GROUP OF EVOLUTIONARILY CONSERVED DEVELOPMENTAL REGULATORS

Although the *COP/DET/FUS* genes were identified by their role in light-regulated development in Arabidopsis, homologous genes have been found in other organisms, including human, mouse, and *Caenorhabditis elegans*, mostly through genome sequencing (Chamovitz and Deng, 1995). Although these findings have not necessarily provided additional clues for the specific functions of these genes, it suggests that they may play roles in the development of other organisms. It is particularly worth noting

that Arabidopsis COP9 and COP11, the only two known subunits of the COP9 complex, have a 67 and 65% similarity to the human counterparts, respectively, across the entire length of the proteins. This degree of conservation may imply a homologous cellular function. It seems possible that the pleiotropic *COP/DET/FUS* genes represent an evolutionarily conserved group of developmental regulators, which in higher plants were recruited to regulate photomorphogenic development. Perhaps the knowledge gained from the studies of these pleiotropic *COP/DET/FUS* genes will provide guidance for understanding the function of their human counterparts.

CONCLUDING REMARKS

Although the initial genetic identification of the pleiotropic *COP/DET/FUS* genes was reported more than 30 years ago (Müller, 1963), the recent rediscovery of this class of genes in photomorphogenic screens resulted in significant advances in our understanding of their physiological and cellular functions. Genetic, molecular, and cell biological studies have not only revealed the molecular identity of four of these genes but also led to many insights concerning their roles in light-regulated development, including cellular localization of action, possible light regulation, and functional interactions. These advances should provide fertile ground for future studies designed to elucidate the overall regulatory network and to understand the molecular interactions involved. Many obvious questions need to be answered: What are the interaction partners of the gene products already identified? What are their biochemical interactions and activities? How do they regulate their downstream targets? How are light signals from multiple receptors integrated to modulate their activities? How do they relate to those light-signaling components such as trimeric G proteins, Ca^{2+}/calmodulins, and cGMP (Bowler and Chua, 1994), which are defined biochemically. Indeed, the most exciting time is yet to come.

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