IN THIS ISSUE

Vampire Plants?

Among the most visible symptoms of the human skin disorder porphyria cutanea tarda are disfiguring light-induced blisters that can lead to extensive scarring and skin discoloration. Individuals suffering from severe cases of this and other forms of porphyria may exhibit excessive hair growth on their face and hands, gum degeneration, and neurological disorders. To manage their disease, porphyria patients need to stay out of the sun and should avoid a range of chemicals that can aggravate the symptoms, including certain metabolites that accumulate in garlic. One course of treatment includes repeated blood transfusions. These symptoms, disease management strategies, and treatments are clearly reminiscent of characteristics typically associated with vampires and werewolves, and it is widely assumed that folkloric reports of such beasts may, in fact, be based on the suffering of unfortunate individuals afflicted with porphyria.

In many cases, porphyria cutanea tarda is triggered by dominant mutations in the gene encoding the enzyme uroporphyrinogen decarboxylase (UROD; Whitby et al., 1998). UROD catalyzes the fifth step on the porphyrin biosynthetic pathway, which provides precursors for the synthesis of heme-containing molecules such as hemoglobin and, in plants, chlorophyll (von Wettstein et al., 1995). Because they possess only 50% of wild-type UROD levels, mutant skin cells accumulate the enzyme’s immediate precursor, uroporphyrinogen. This molecule becomes highly reactive when it is activated by light, to the extent that it is capable of donating energy or electrons to molecular oxygen. The resulting reactive oxygen species (ROS) cause extensive damage to skin cells and can eventually kill them.

What is this description of a human medical condition doing in THE PLANT CELL? Following last month’s demonstration by López-Solanilla et al. (1998) that bacterial pathogens of plants and animals use a common suite of gene products to counteract antimicrobial peptides produced by their respective hosts, there is emerging evidence that genetic diseases of plants and animals can also exhibit parallels. Indeed, in the case presented by Hu et al. on pages 1095-1105 of this issue, the parallels are especially clear. These authors demonstrate conclusively that dominant mutations at the Les22 locus fall in the maize Urod gene, and as a consequence, that the mutant plants accumulate uroporphyrinogen in their leaf cells. In other words, Les22 mutants suffer from a condition that is entirely analogous to porphyria cutanea tarda.

On the face of it, this finding is somewhat surprising. The authors’ initial interest in Les22 was piqued by the fact that it is a member of a large class of “lesion mimic” mutants, so called because they spontaneously develop discrete necrotic lesions that are similar in color and shape to those formed during some plant defense responses. These similarities underlie the not unreasonable assumptions that many lesion mimic mutants may have defects in genes that affect signaling or responses during plant-pathogen interactions or that control cell-death pathways to restrict lesion spread (see, e.g., Dangl et al., 1996; Buckner et al., 1998).

These assumptions have been reinforced by recent breakthroughs establishing direct mechanistic links between lesion mimic mutations and pathogenesis or pathways that control cell death. For example, Hu et al. (1996) showed that recessive mutations in the maize disease resistance gene rp1 trigger the formation of spontaneous lesions, whereas Büschges et al.’s work on Mlo in barley (Büschges et al., 1997) and Gray et al.’s work on Lethal leaf spot1 in maize (Gray et al., 1997) appear to have uncovered two novel negative regulators of plant cell-death pathways. Furthermore, Jabs et al. (1996) have shown that mutations in the Arabidopsis LESIONS SIMULATING DISEASE1 (ps11) gene, which was recently cloned (it encodes a putative transcription factor; Dietrich et al., 1997), provoke uncontrolled cell death that is initiated by superoxide radicals.

Nevertheless, Les22 is not the only well-characterized lesion mimic mutant in which genetic, molecular, and/or biochemical analyses indicate that the lesion mimic phenotype is a secondary consequence of the mutation. Indeed, it is now abundantly clear that the analysis of lesion mimic mutations should be approached with an appreciation for the broad range of different cell biological and developmental pathways that may be affected. For example, some lesion mimic phenotypes are developmentally regulated (as are some plant defense responses; see, e.g., Hammond-Kosack and Jones, 1996) and many more are only triggered when the mutant plants are exposed to light (Buckner et al., 1998).

One light-dependent lesion mimic, psi2 (phytochrome signaling intermediate 2), was described by Genoud et al. in the June issue of THE PLANT CELL (Genoud et al., 1998). The genetic analyses performed by these authors suggest that the primary defect in the psi2 mutant is not in cell-death signaling pathways but instead in phytochrome-mediated light signal transduction (Genoud et al., 1998). They hypothesize that PSI2 may encode or affect the activity of a negative regulator of phytochrome signaling pathways, and, in a striking congruence with Hu et al.’s work, they suggest that a build up of signaling intermediates in
the mutant may trigger cell death in a manner that is analogous to certain retinal neurodegenerative diseases in animals.

Light is also required for full expression of the lesion mimic phenotype in Les22 mutants. Indeed, in their detailed analyses of the phenotypes conditioned by mutations in Les22, Hu et al. show that lesions do not develop in leaf regions that are shielded from light. Moreover, they also demonstrate that if these regions remain shielded for protracted periods, they become impervious to lesion formation even after they are returned to the light. This observation suggests that there is some level of developmental control of lesion formation in Les22—perhaps individual cells are only susceptible to high uroporphyrinogen levels for a brief window of developmental time. Alternatively, flux through the entire chlorophyll biosynthetic pathway may decrease as leaves mature to the point at which a 50% reduction in UROD levels no longer causes a harmful buildup of uroporphyrinogen.

The authors’ analyses of Les22 mutants have also uncovered a recessive “yellow seedling lethal” (ysl) phenotype that is exhibited by Les2 homozygotes. These seedlings are yellow when they germinate, and because they are unable to green, they do not survive for long. Hu et al. suggest that this novel phenotype also results from defects in porphyrin biosynthesis. However, in this case, the vastly decreased levels of UROD in the homozygous mutant seedlings are likely to be manifested as a complete block in the porphyrin biosynthetic pathway. This block impedes both chlorophyll and heme biosynthesis, explaining the lethality of the homozygous condition.

Although it is lethal to the plants, the recessive ysl phenotype has allowed the authors to characterize the genetics of Les22 in more detail. Indeed, they report preliminary indications that the 17 independent but closely linked Les22 mutations, which they initially identified as Robertson’s Mutator (Mu)-induced dominants, may actually map to three distinct complementation groups.

With all these transposon-induced mutations in hand, it was a less than usually complicated job for Hu et al. to identify Mu-containing restriction fragments that cosegregate with the lesion mimic phenotype and, thereafter, to clone the affected gene. With the Les22 sequence in hand, a brief series of computer-based searches afforded Hu et al. the most obvious molecular explanation for the phenotype provoked by this mutation—that Les22 plants are suffering from a plant form of porphyria (the authors suggest dubbing the condition phytoporphyrinosis). Because they have only one active copy of the Urod gene, levels of the photoactive uroporphyrinogen intermediate increase in their cells (Hu et al. confirm such a buildup biochemically). This buildup triggers ROS production and the restricted leaf cell death that is typical of lesion mimic mutants.

A similar conclusion was drawn recently by Mock and Grimm (1997; see also Mock et al., 1998) following their analyses of tobacco plants expressing an antisense version of the Urod gene. These transgenic plants develop lesions as well as a range of other phenotypes, and they will therefore provide a useful source of material for continued analyses of the role of porphyrin intermediates in lesion formation (Mock and Grimm, 1997; Mock et al., 1998).

These findings have a number of implications for analyses of plant disease resistance responses and the role of lesion formation in these responses. In setting the metabolic cat among the pathogenic pigeons, Hu et al.’s work confirms that lesions can form as a result of mutations in genes that affect a number of different processes in the plant, from metabolism and ROS production to light signaling and the control of cell death. Their data strongly imply that other lesion mimic phenotypes may also result from metabolic pathway defects, and it is not difficult to imagine that mutations in any gene that result in the accumulation of photoactive metabolites may provoke lesion formation. Some lesion mimic mutations may even occur in genes encoding other porphyrin biosynthetic enzymes, a hypothesis for which there is precedence in humans (see, e.g., Frank et al., 1998) and plants (Mock and Grimm, 1997; Mock et al., 1998).

Moreover, Hu et al.’s demonstration that the lesion mimic phenotype provoked by mutations in Les22 is the result of a 50% decrease in levels of a metabolic enzyme uncovers a rare case of haploinsufficiency in plants. However, given that many other lesion mimic phenotypes share genetic and developmental characteristics with those provoked by mutations in Les22, it is possible that haploinsufficiency may turn out to be the rule rather than the exception, at least for lesion mimics.

Nevertheless, many questions regarding the nature of the lesions that form spontaneously in these mutants and those that comprise one component of a plant’s defense responses remain to be resolved. One of the most intriguing and pressing of these questions is, what controls lesion initiation and spread? After all, the cells in Les22 mutants are presumably all genetically identical (with the exception of those in which the Mu element has moved out of the Urod gene), yet cell death is triggered in only a few. One attractive hypothesis that the authors develop from a suggestion made by Martenssen (1997) is that individual leaf cells may have differential abilities to detect, resist, and/or respond to the production of ROS by their neighbors. Thus, although a few cells may die after ROS levels go up, developmentally distinct cells, despite being in close proximity to the dying cells, may not.

Clearly, work on lesion mimics can be of profound practical importance. In this case, for example, it is possible that UROD levels could be manipulated in transgenic plants in such a way that they develop discrete lesions in the immediate vicinity of an attacking patho-
The potential feasibility of using antisense Urod constructs to reduce UROD levels has already been demonstrated in tobacco (Mock and Grimm, 1997; Mock et al., 1998) and it is tempting to speculate that similar approaches may prove effective in efforts to generate crop plants exhibiting broad-spectrum pathogen resistance.

In combination with the work on other lesion mimic mutants that is going on in many other laboratories, Hu et al.’s continued analysis of Les22 is sure to provide additional novel and/or unexpected insights into the molecular and biochemical bases for disease lesion mimicry. In turn, it is clear that these investigations will impinge on many aspects of plant biology, including plant–pathogen interactions, light signaling, cell death, and leaf development. Experiments with Les22 may also impact medical research. Indeed, it is conceivable that research on the porphyrin biosynthetic pathway in maize and tobacco could one day contribute to the development of effective treatments for porphyria in humans.

Crispin B. Taylor

REFERENCES


Vampire Plants?
Crispin B. Taylor
Plant Cell 1998;10;1071-1073
DOI 10.1105/tpc.10.7.1071

This information is current as of October 27, 2017

References
This article cites 16 articles, 11 of which can be accessed free at:
/content/10/7/1071.full.html#ref-list-1

Permissions

eTOCs
Sign up for eTOCs at:
http://www.plantcell.org/cgi/alerts/ctmain

CiteTrack Alerts
Sign up for CiteTrack Alerts at:
http://www.plantcell.org/cgi/alerts/ctmain

Subscription Information
Subscription Information for The Plant Cell and Plant Physiology is available at:
http://www.aspb.org/publications/subscriptions.cfm