the relative resistance of a small fraction of the population to acquired immunodeficiency syndrome (AIDS), in itself a massive experiment on human natural selection.

Several speakers speculated on the developments that the study of life might witness in the next 50 years: cures for still-intractable infectious diseases, a deeper understanding of the origins of life, a reasonable insight into how the brain works, and the emergence of a blueprint for the development of organisms are all on the agenda. All agreed that an increasing proportion of biologists' time will be spent on experiments *in silico*, that is, by computer modeling. The discussions on the fate of the species, and indeed of the planet, were rather more pessimistic. Manfred Eigen, Nobel laureate and director of the Max Planck Institute in Göttingen, wove together the future of biology and the future of the planet. Of the many serious problems confronting humans, the most urgent is that of population growth. According to Eigen, to feed the world's population in 50 years' time will require all our ingenuity, including the use of nuclear power and genetic engineering to increase crop yields. He urged scientists to become involved in the great debates on these subjects that currently grip society, and he emphasized that time is of the essence: We do not have much time left to prove that we are not the products of a lethal mutation.

Reference

1. The meeting "What Is Life?" was held in Dublin, Ireland, on 20 to 22 September 1993.

Surprising Signals in Plant Cells

Alan M. Jones

Plants, like animals, must respond to environmental cues. In the past few months, some surprising specifics of how plants perceive and transduce these signals have come to light. Working independently, four research groups have found new signal perception mechanisms in plants not described before for any eukaryotic cell: We now know something about how plants sense blue light and the plant hormones salicylic acid, ethylene, and the class of growth-promoting hormones designated as auxins, of which indole-3-acetic acid is the representative member.

Salicylic Acid

In *Science*, Chen and co-workers of the Klessig group (*1*) reported the identity of a receptor for salicylic acid, the endogenous signal required for the systemic acquired resistance (SAR) response of plants. SAR is part of a defense response that is induced locally by pathogen or pest attack but that spreads systemically to protect the entire plant. Salicylic acid likely mediates this response: Application of salicylic acid or certain analogs such as aspirin (acetylsalicylic acid) induces the rapid expression of the pathogenesis-related genes, which serve as molecular markers for the SAR response (*2*). Moreover, the timing is right. Salicylic acid increases throughout the plant after only one part of the plant is attacked by a pathogen, and this increase occurs before the expression of the pathogen-related genes (*3*).

Chen and co-workers found that the cellular binding protein for salicylic acid shares high sequence identity with some members of the catalase family of enzymes (*1*). Catalases reduce and effectively inactivate hydrogen peroxides, one type of reactive oxygen species (ROS) in eukaryotic cells. Could this member of the catalase family be the salicylic acid receptor that mediates the SAR response? Several pieces of evidence suggest that it is. The binding of salicylic acid to catalase is regulatory and inhibits its enzymatic activity, at least in vitro. The resulting increase in ROS could possibly activate specific transcription factors, as active oxygen species do in animal cells (*4*). Chen and co-workers therefore tested whether pathogen-related gene expression is increased by the addition of compounds that increase the amounts of ROS in the cell. Their results suggest that ROS can induce pathogen-related gene expression. Other data also point to the induction of SAR by salicylic acid as being mediated through catalase: The binding affinity of salicylic acid and its analogs to catalase parallels the inhibitory action of these compounds on hydrogen peroxide reduction and, of critical importance, parallels their ability to induce SAR. This observation links the action of catalase to SAR, thereby diminishing the trivial possibility that salicylic acid and its analogs are nonspecifically binding to catalase (for example, by the ability of salicylic acid to chelate the iron cofactor of catalase).

That ROS may transduce the signal that mediates the response to pathogen attack fits with the observation that extracellular ROS elicit local defense mechanisms. Triggers of SAR such as fungal cell wall glycans and glutathione cause local oxidative crosslinking of cell wall proteins well in advance of the effect on gene transcription (*5*). This is the first action of the plant in response to a pathogen attack—erection of a local barricade by stiffening of the cell wall through intermolecular crosslinks. Thereafter, the plant systemically induces defense- and wound-related genes that provide further resistance. Both actions are mediated by ROS. These ROS, although certainly toxic at high concentrations, now must be considered true secondary messengers when present at lower concentrations. We may even eventually find that ROS are important messengers for growth and development as well.

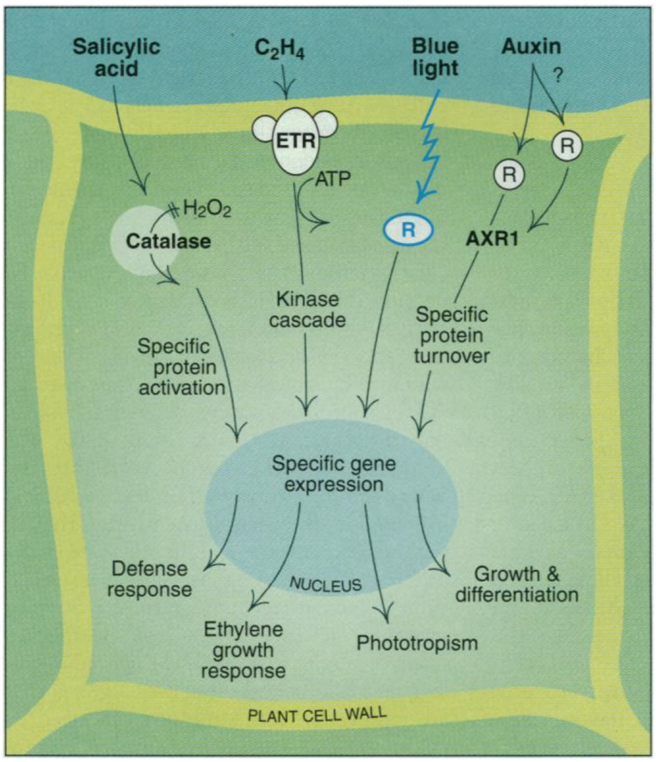

ILLUSTRATION: K. SUTLIFF

Surprising signals. The recently discovered mechanisms by which plants sense their environments.

The author is in the Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599–1280.

Ethylene

The gas ethylene has been known since the turn of the century as a plant hormone, most notably as a signal for fruit ripening but also for growth regulation of certain plant organs (*6*). Because of ethylene's gaseous nature, traditional methods for identifying and isolating the ethylene receptor have progressed slowly. Consequently, Chang and co-workers (*7*) took a genetic approach and cloned the *Etr* gene responsible for ethylene sensitivity in *Arabidopsis* (*7, 8*). This *Etr1* gene shares sequence identities with a class of prokaryotic proteins that are components of the two-component signal transduction system, proteins responsible for detection of simple molecules in the periplasmic space. ETR1 may be the ethylene receptor or a component of the receptor because it has several features consistent with receptor function: ETR1 is the furthest upstream in the response pathway, has transmembrane sequences, and, when deficient, reduces ethylene binding in etr mutant plants. However, more biochemical data are needed to be certain. The identification of all the molecules in the ethylene signal pathway awaits further acquisition and characterization of ethylene mutants. The available mutants have been used to establish the epistasis of these gene products. ETR1 lies at or near the beginning of the ethylene perception pathway, consistent with its proposed receptor function. Downstream of ETR1 is CTR1 (*10*), a protein similar to members of the Raf family of serine-threonine protein kinases. Soon to follow is the molecular identification of other genes in this pathway—such as *Ein2* and *Ein3*—which will add considerably to our understanding of the ethylene signal pathway.

Blue Light

Blue light regulates the growth and morphology of plants, but is best known as the signal for phototropism, the ability of plants to grow toward light. The blue light receptor, predicted to be a flavoprotein, has been difficult to isolate and characterize biochemically, largely because of its low concentrations in the cell. But, as for the ethylene perception pathway, a genetic approach has recently permitted researchers to surmount this biochemical barrier. The *hy4* mutant of *Arabidopsis* (*11*), isolated over a decade ago, is insensitive to blue light. By screening for a *hy4* allele tagged with a T-DNA insertion, Ahmad and Cashmore (*12*) were able to isolate the wild-type gene, which encodes a protein with significant sequence identity to prokaryotic DNA photolyases, flavoproteins that repair DNA damaged by ultraviolet light. Although the chromophore-binding domain of HY4 shares homology to photolyase, HY4 most likely does not repair DNA, and its mode of action is unknown. Elucidating its mechanism of action will require extensive investigation, but there is reason to believe already that this signal pathway will prove to be unique.

Auxins

Because auxins regulate so many aspects of plant development—cell division, elongation, and differentiation—it has often seemed that it might be impossible to obtain viable auxin receptor mutants or that the phenotypes of such mutants might be unpredictable. The *axr1* mutant of *Arabidopsis* is insensitive to auxin and has the same characteristics as a plant that contains low concentrations of auxins. However, mutant plants contain the same amount of auxin as a wild-type plant, suggesting that the lesion in *axr1* lies close to auxin perception in this signal transduction pathway (*13*). Leyser and co-workers of the Estelle group recently reported the cloning and sequence of the *axr1* gene (*14*). Surprisingly, AXR1 shares sequence identity with the E1 enzyme of the ubiquitin activation pathway, a pathway that tags proteins for a certain type of degradation. E1 covalently binds the small protein ubiquitin at a cysteine in an adenosine triphosphate (ATP)–dependent fashion, then transfers ubiquitin to the E2 enzyme, which subsequently transfers the ubiquitin tag to a protein targeted for degradation in a protease complex known as the proteasome (*15*). Although ubiquinated proteins are typically degraded rapidly, some—such as the T cell antigen and platelet-derived growth factor receptor—are ubiquinated in a ligand-dependent manner, possibly as a regulatory modification. Indeed, a role for ubiquitin in growth control has recently been established (*16*). However, it is not clear whether AXR1 could be an active E1 enzyme, because it is truncated and lacks critical motifs such as the ATP binding sites and the conserved cysteine residue to which ubiquitin is attached. Consequently, AXR1 is probably a novel element in a signal transduction chain. How could the ubiquitin activation reactions fit into the auxin signal pathway? If indeed AXR1 is involved in the ubiquitin pathway, then it perhaps controls the stability of some of the other elements in auxin signal transduction. For example, rapid turnover of transcription factors is crucial for the mechanism of auxin action. Theologis and colleagues (*17*) recently found two genes that are rapidly (within 5 minutes) induced by auxin and that encode proteins with a predicted structure similar to that of some prokaryotic DNA binding proteins. These putative transcription factors are rare proteins with half-lives of 6 to 8 minutes, perhaps the shortest lived proteins discovered to date. Because the genes encoding these transcription factors are expressed when protein synthesis inhibitors are added, regulation of gene expression by a short-lived, hormone-dependent repressor has been proposed to explain the observation. Perhaps there is a connection between the rapid turnover of these short-lived factors and AXR1, a putative member of the protein-turnover pathway.

Increased efforts toward elucidating plant cell biology are identifying new kinds of receptors and signal transduction pathways for eukaryotic cells. Some of these mechanisms may be unique to plants and have evolved to sense the changing environment, but most of these new discoveries will undoubtedly be confirmed and extended in other eukaryotic cells.

References

1. Z Chen, H Silva, D. F Klessig, *Science* **262**, 1883 (1993).
2. E R. Ward *et al.*, *Plant Cell* **3**, 1085 (1991), I. Raskin, *Annu. Rev. Plant Physiol. Plant Mol Biol.* **43**, 439 (1992), *Plant Physiol.* **99**, 799 (1992), J Malamy and D Klessig, *Plant J* **2**, 643 (1992).
3. J. Malamy, J. P Carr, D F. Klessig, I Raskin, *Science* **250**, 1002 (1990), J P. Métraux *et al.*, *ibid.*, p. 1004
4. R. Schreck and P. A Baeuerle, *Trends Cell Biol* **1**, 39 (1991)
5. D. J Bradley, P Kjellbom, C. J. Lamb, *Cell* **70**, 21 (1992); V P Wingate, M A. Lawton, C. J. Lamb, *Plant Physiol.* **87**, 206 (1988).
6. H Kende, *Annu. Rev. Plant Physiol Plant Mol. Biol.* **44**, 283 (1993); F B. Abeles, P W. Morgan, M E. Saltveit, *Ethylene in Plant Biology* (Academic Press, New York, 1992), A. K Mattoo and J. C. Suttle, *The Plant Hormone Ethylene* (CRC Press, Boca Raton, FL, 1991)
7. C. Chang, S. F. Kwok, A. B. Bleeker, E. M. Meyerowitz, *Science* **262**, 539 (1993).
8. A. B Bleeker, M. A. Estelle, C. Somerville, H. Kende, *ibid.* **241**, 1086 (1988).
9. D. E Koshland Jr, *ibid* **262**, 532 (1993), J. S. Parkinson, *Cell* **73**, 857 (1993)
10. J. J. Kieber *et al.*, *Cell* **72**, 427 (1993); P Guzman and J R. Ecker, *Plant Cell* **2**, 513 (1990); V. Raz and R. Fluhr, *ibid* **5**, 523 (1993).
11. M. Koorneef, E Rolff, C J. P Z. Spruit, *Z. Pflanzenphysiol.* **100**, 147 (1980).
12. M. Ahmad and A R. Cashmore, *Nature* **366**, 162 (1993).
13. M. Estelle and C R. Sommerville, *Mol Gen. Genet.* **206**, 200 (1987); C. Lincoln *et al.*, *Plant Cell* **2**, 1071 (1990).
14. H M. Ottoline Leyser *et al*, *Nature* **364**, 161 (1993).
15. D. Finley and V. Chau, *Annu Rev Cell Biol.* **7**, 25 (1991); A. Hersko and A. Ciechanover, *Annu Rev. Biochem.* **61**, 761 (1992); A. Varshavsky, *Cell* **69**, 725 (1992).
16. C. Cenciarelli *et al*, *Science* **257**, 795 (1992); S. Mori, C -H. Heldin, L. Claesson-Welsh, *J Biol Chem.* **267**, 6429 (1992); F Papa and M. Hochstrasser, *Nature* **366**, 313 (1993).
17. S Abel, P. W Oeller, A Theologis, *Proc. Natl. Acad. Sci U S A.* **91**, 326 (1994)