for activators, necessary only to escort TBP to the promoter? This possibility seems unlikely, considering how highly conserved the TAFs are over evolution and their number (8 to 10 at least). It is likely that there are other structural and functional roles for TAFs, and further experiments will undoubtedly uncover these functions. Indeed, some TAFs make DNA contacts and contribute to promoter recognition. Upcoming genetic experiments in *Drosophila* and yeast will be critical for evaluating the in vivo roles of the TAF proteins.

Several reports suggest that TFIID responds to activators with conformation changes that occur after binding to the promoter. These changes are thought to facilitate subsequent interactions of other basal factors such as TFIIB and polymerase (*3*). These models of activator function are not inconsistent with increased TFIID recruitment. In fact, both recruitment and conformation changes could be mediated by the same activator-TAF contacts.

If the TAFs are essential for response to activators, are they sufficient? The experiments of Sauer *et al.* are done with highly purified factors, suggesting that only TAFs and the basal factors are necessary for activator responsiveness. Other factors can potentiate the response to activators in vitro, including TFIIA and several positive and negative cofactors (*3*, *4*). The activity of these factors is apparently still dependent on TAFs. In addition, a substantial body of genetic and, more recently, biochemical evidence points to chromatin as an essential regulator of gene expression. Repression and derepression, as opposed to an actual increase in the rate of transcription, probably account for many of the observed effects of these additional factors. Nevertheless, it is essential to determine whether these other transcription regulators modulate the TAF-based activation process or function in independent pathways of gene activation.

Another set of factors important for gene regulation are those recently identified as components of a yeast mediator (or holoenzyme) complex (*5*). This set of proteins was originally identified genetically as suppressors of mutations in RNA polymerase II, and biochemical analysis revealed that the complex was associated with RNA polymerase II and one or more of the basal transcription factors. The holoenzyme contains several proteins implicated in gene regulation by yeast genetics. Surprisingly, this complex responds in vitro to transcription activators in the presence of TBP, implying the existence of a TAF-independent mechanism for transcription regulation. Like TAF-dependent activation, holoenzyme-mediated activation may be due to stabilizing contacts between the transcription regulators and holoenzyme components (*6*).

How are the basal trascription factors delivered to a promoter? Until recently, it was assumed that a stepwise assembly of basal factors would provide multiple points for regulation. In another view, the holoenzyme model, some or all basal factors are preassociated before reaching the promoter. If an entire transcription complex was assembled off the DNA, it would present only a single, extremely large target for activators. A recently described mammalian holoenzyme preparation apparently carries all the essential basal transcription factors (*7*) but, unexpectedly, does not respond to activators.

Many prokaryotic activators stimulate transcription either by recruiting the holoenzyme to the promoter or by increasing DNA strand separation at the initiation site. It is likely that eukaryotic activators can also affect multiple steps in initiation. The TAF-dependent activation described by Sauer *et al.* (*1*) is mechanistically similar to the first class of bacterial activation. Activator-induced conformation changes in the eukaryotic transcription complex also seem likely, but more work is required. Although partial answers are emerging, deciphering the mechanisms of activator function will remain a central goal of the field for some time.

References

1. F. Sauer, S. K. Hansen, R. Tjian, *Science* **270**, 1782 (1995); *ibid.*, p. 1825.
2. S. Chatterjee and K. Struhl, *Nature* **374**, 820 (1995); N. Klages and M. Stubin, *ibid.*, p. 822.
3. B. Choy and M. R. Green, *ibid.* **366**, 531 (1993); T. Chi, P. Lieberman, K. Ellwood, M. Carey, *ibid.* **377**, 254 (1995).
4. M. Meisterernst, A. L. Roy, H. M. Lieu, R. G. Roeder, *Cell* **66**, 981 (1991).
5. A. J. Koleske and R. A. Young, *Nature* **368**, 466 (1994); Y. J. Kim *et al.*, *Cell* **77**, 599 (1994).
6. A. Barberis *et al.*, *Cell* **81**, 359 (1995).
7. V. Ossipow, J. P. Tassan, E. A. Nigg, U. Schibler, *ibid.* **83**, 137 (1995).

UPDATE

Ethylene Sensors: How Perceptive!

Athanasios Theologis

Ethylene (C_2H_4), a multipurpose signaling molecule in plants (*1*), orchestrates vital growth stages such as fruit and flower senescence and defense against pathogens. As reviewed previously in *Science*, its receptor and transduction apparatus are just emerging into view (*2*); now two new studies on ethylene sensors (*3*, *4*) put the receptor into even sharper focus.

Plants sense ethylene by a protein kinase cascade (*2*, *5*). *CTR1* and *ETR1*, two *Arabidopsis* genes essential for ethylene signaling, encode a putative RAF-like serine-threonine protein kinase (*6*) and a putative histidine protein kinase similar to the prokaryotic, two-component sensors. Without functional ETR1, plants do not bind ethylene effectively; ETR1 acts upstream of CTR1 and other components in the pathway (*2*). So the ETR1 protein has been proposed as the ethylene receptor (*7*). And indeed it is—as shown by Schaller and Bleecker on page 1809, where they demonstrate that ETR1 binds ethylene.

When ETR1 was first described, it seemed to be the only ethylene receptor; but then a second ethylene sensor, ERS, was isolated from *Arabidopsis* (*8*). An ERS mutation confers dominant ethylene insensitivity to wild-type *Arabidopsis* (*8*). But the excitement does not end there. On page 1807 of this issue, H. Klee's laboratory reveals that the old and forgotten tomato ripening mutant *Nr* is the result of a dominant mutation in the transmembrane domain of the NR protein (an ERS-like gene product). More importantly, a transgenic yeast strain expressing the wild-type NR protein also binds ethylene (*9*). At the same time, M. Tucker's laboratory at the USDA in Beltsville, Maryland, cloned an ETR1 homolog from tomato (*10*). The tomato eTAE1 (*ETR1*) mRNA is expressed during flower and fruit senescence, whereas the NR (*ERS*) mRNA is developmentally regulated during fruit ripening (*4*). The picture that emerges is that ethylene sensors are encoded by multigene families with members that are differentially expressed during plant growth and development.

The author is at the Plant Gene Expression Center, 800 Buchanan Street, Albany, CA 94710, USA.

References

1. F. B. Abeles, P. W. Morgan, M. E. Saltveit Jr., *Ethylene in Plant Biology* (Academic Press, San Diego, 1992).
2. J. R. Ecker, *Science* **268**, 667 (1995).
3. G. E. Schaller and A. B. Bleecker, *ibid.* **270**, 1809 (1995).
4. J. Q. Wilkinson, M. B. Lanahan, H.-C. Yen, J. J. Giovannoni, H. J. Klee, *ibid.*, p. 1807.
5. C. Chang, *Trends Biochem. Sci.*, in press.
6. J. J. Kieber, M. Rothenburg, G. Roman, K. A. Feldmann, J. R. Ecker, *Cell* **72**, 427 (1993).
7. C. Chang, S. F. Kwok, A. B. Bleecker, E. M. Meyerowitz, *Science* **262**, 539 (1993).
8. J. Hua, C. Chang, Q. Sun, E. M. Meyerowitz, *ibid.* **269**, 1712 (1995).
9. A. Bleecker, personal communication.
10. D. Zhou, A. K. Mattoo, M. L. Tucker, *Plant Mol. Biol.*, in press.