new set of target genes.

A relatively small domain of E2F, consisting of 18 amino acids that reside at the extreme carboxy terminus of the protein (residues 409–426), seems to be responsible for the interaction with Rb. The Rb-binding domain also overlaps with sequences that are essential for transcriptional activation, which represent the carboxy-terminal 60 amino acids, at least when assayed in GAL4 fusion constructs. Given this overlap, a simple mechanism for Rb control of E2F function could be envisaged whereby the Rb protein would mask the activation domain, blocking the ability of E2F to interact with the transcriptional machinery and stimulate transcription (see figure). In fact, transfection experiments have shown that the interaction of Rb with E2F, although having no effect on DNA binding, inhibits the ability of E2F to stimulate transcription[11].

Common pathway

This brings us back to the question of why E2F, and the interaction of E2F with proteins such as Rb, is sitting at the centre of a common pathway targeted by the DNA virus oncoproteins. One possible answer comes from the identification of cellular genes that appear to use E2F. Many of them encode proteins that are essential for S phase in the cell cycle, including dihydrofolate reductase (DHFR), thymidine kinase and DNA polymerase α. Moreover, the E2F sites in the DHFR promoter are essential for activation of DHFR in late G1 (ref. 12). Uncomplexed, and presumably transcriptionally active, E2F accumulates at this time[13]. So a common strategy of the DNA tumour viruses may be to activate E2F, and thus S-phase gene expression, in otherwise quiescent cells to provide the necessary environment for viral DNA synthesis.

Simple stories usually become more complicated before they are finished. The finding[7] that only the underphosphorylated form of Rb was bound to E2F, an observation now also made with the cloned E2F protein, led to the speculation that E2F was inactive in G1, as a consequence of sequestration by Rb, and was then released as an active factor in late G1 when Rb became phosphorylated. Although uncomplexed E2F does accumulate at the end of G1, release of the E2F–Rb complex does not appear to be the source because the E2F interaction with Rb persists through S phase (ref. 14 and unpublished observations of my own group). There is a G1-specific E2F complex[13] that could be a source of this E2F, but this complex does not involve Rb. New synthesis of E2F might also contribute under some circumstances, as Kaelin *et al.*[3] found that the RNA detected by the *RBAP-1* cDNA was at low levels in quiescent T cells and then accumulated following mitogen stimulation.

But what, then, is the functional significance of the Rb–E2F interaction if it does not serve as a reservoir for E2F? One possibility is that Rb bound to E2F does not simply sequester E2F, but that this complex actively represses the transcription of certain target genes. Indeed, experiments reported earlier this month in *Nature*[15] point to this possibility. Two potential targets for control by E2F–Rb are the *c-myc* gene and the *cdc2* gene — transfection assays demonstrate that Rb can repress *c-myc* transcription as well as *cdc2* transcription, dependent on E2F sites in the respective promoters[16,17].

Finally, as if the array of interactions involving E2F were not complicated enough, E2F is also found in association with the Rb-related p107 protein, together with the cyclin A–cdk2 kinase complex, during S phase[14,18,19]. This association thus generates a cyclin-dependent protein kinase that has sequence-specific DNA-binding activity, an interesting property for a kinase that is suspected to be involved in the events of S phase. Although it seems unlikely that the complex would be essential for the initiation of S phase, given that transformed cells lacking the complex certainly do enter S phase, a role at the end of S phase in controlling the entry into mitosis is a possibility. Clearly, one payoff of the cloning of E2F will be the generation of reagents that should provide answers to questions as to the precise function of E2F in these events. Regardless of the details, it is already clear that this transcription factor is a central figure in the control of cell proliferation, gaining the attention of a variety of cellular and viral regulatory proteins — not to mention a few scientists. □

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DAEDALUS

Wood for ever!

A TREE, says Daedalus, is only alive on the outside. Every year it grows another circumferential surface layer of living wood, while the layer beneath dies. The central wooden core is only a passive support; even if it rots, the resulting hollow tree can continue to flourish. So it should be possible to remove a hollow core from a tree every year, and trust to the inward pressure of next year's growth to squash the central hole back to its original size, ready to yield another hollow core.

This subtle concept of 'continuous forestry' deserves to be elaborated. Daedalus plans to plant a line of trees close together, like close-packed railings in a fence. He will chop off all branches which grow in the plane of this fence; as the trunks themselves grow and make mutual contact, he will shave the bark along the contact line and join the living wood beneath with grafting wax. The line of trees should ultimately graft completely together, fusing into a sort of 'planar tree' with branches sticking out on either side of it.

The next stage of the operation will be rather tricky. The planar tree will be sawn vertically down its long axis, separating it into two half planes. Each will have bark and branches on its front face, while its raw wooden back face will abut that of its twin. One half plane will be uprooted, moved a few metres back, and replanted. The resulting parallel wooden walls will resemble the front and back walls of a house. The enclosure will be completed by transplanting a second pair of tree half planes into place as side walls, and adding a suitable greenhouse-type roof.

The result will be a sort of huge square hollow tree-house with a sheltered interior. New wood will be steadily laid down on the living outer surface, and will displace the inner dead layers into the house. The warm, dry atmosphere within will season them to perfection. Every few years or so, a thick layer will be planed off the inner walls of the house and manoeuvred out of a vertical exit slit left in one corner. An endless supply of huge, ready-seasoned wooden sheets will be obtained, far larger than the narrow rectangular planks yielded by chopping down a natural tree, and without the waste imposed by its circular cross-section.

Trees have no natural lifespan; once established, an estate of tree-houses should survive indefinitely. Nothing need ever be cut down. The clusters of living, branched, leafy, but recognizably rectangular houses will have a fantastic, magical look, like something out of Hans Andersen. They could even be let as dwellings. The ideal tenants would be witches, lost children and enchanted princesses. David Jones