changeable substrate receptors for SCF ubiquitin ligases[10]. The hypothetical 'CSN proteasome' may recognize a subset of proteins, including COP1 targets such as HY5. However, a subunit of the lid was recovered in a two-hybrid screen for *Arabidopsis* proteins that bind to CSN1 (ref. 11). Thus, rather than replacing the lid, CSN may in fact bind to the intact 26S proteasome. This observation supports the second hypothesis, that CSN and the 26S proteasome may act in series to mediate the degradation of specific substrates.

How might CSN facilitate the destruction of COP1 targets? CSN and the lid each contain two subunits containing MPN domains and six subunits possessing PCI motifs[8,9]. We propose that one of these domains comprises a tetra-ubiquitin-binding motif (tetra-ubiquitin is the shortest multi-ubiquitin chain that efficiently targets a substrate to the 26S proteasome)[12]. According to this view, both the lid and CSN may bind to several tetra-ubiquitin chains (or to several tetra-ubiquitin segments within a single chain). We envision the following sequence of events (Fig. 2c): COP1 binds to and catalyses the assembly of multi-ubiquitin chains on HY5. Either before or after the ubiquitination step, the COP1–HY5 complex interacts with CSN through direct contacts between CSN, COP1 and ubiquitinated HY5. CSN loaded with the ubiquitin-ligase–ubiquitinated-substrate complex then binds to the lid of the 26S proteasome to deliver its cargo for destruction. If tetra-ubiquitin dissociates quickly from CSN but slowly from the lid, the multi-ubiquitinated substrate could be transferred vectorially from CSN to the lid. Thus, CSN serves to collect ubiquitinated proteins within the nucleus for delivery to the proteasome, possibly protecting them from de-ubiquitination before they can be destroyed. Although this model is highly speculative, it is consistent with all of the available data and is readily testable.

What is next for COP1 and CSN? The biochemical functions of both COP1 and CSN remain to be identified. It also remains unclear how signals from activated photoreceptors impinge on the COP1–CSN axis to relieve repression of HY5. Lastly, it is likely that both COP1 and CSN have other targets and physiological functions in plants and other organisms (for example, a related circuit may control the turnover of TIM and PER during circadian oscillations in animals[13]), but these remain to be discovered. As more and more researchers are beginning to prowl this beat, further suspects should be apprehended shortly. □

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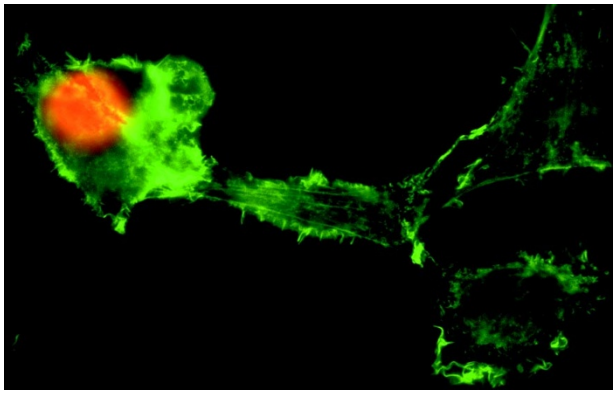
"Eat me" signals of apoptotic bodies

One of the characteristics of apoptotic cell death is the rapid removal of cell corpses, which are engulfed by macrophages or by non-professional phagocytes. This is because induction of cell apoptosis leads to the exposure of "eat me" signals on the cell surface before the late apoptotic event of cell lysis. Thus, apoptosis is a 'clean' process that does not normally lead to spillage of cell contents or to inflammation. Exposure of phosphatidylserine (PS) residues, which are normally asymmetrically distributed and restricted to the inner leaflet of the plasma membrane, has been identified as both an early event in apoptosis and a prerequisite for engulfment, as PS-containing liposomes can inhibit phagocytosis of apoptotic bodies. But what is the receptor for PS on phagocytic cells? Although several cell-surface molecules were proposed to contribute to the recognition of apoptotic cells, none of them seems to bind specifically to PS residues. An alternative model is that recognition is based on homophilic interactions, as exposure of PS on the surfaces of both apoptotic and phagocytic cells has recently been reported to be required for engulfment (Marguet *et al.*, *Nature Cell Biol.* **1,** 454–456; 1999). Now, in a recent issue of *Nature* (**405,** 85–90; 2000), Valerie Fadok and colleagues at the National Jewish Medical and Research Center in Denver, Colorado report the cloning of a PS receptor (PSR), using an antibody raised against activated macrophages, which they found to inhibit engulfment of apoptotic cells. PSR is expressed on macrophages and on certain epithelial cells and fibroblasts. Transfection of the gene encoding PSR confers T and B cells with the capacity to recognize and engulf



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apoptotic cells, which is inhibited by anti-PSR antibodies and by PS-containing liposomes. The picture shows a 3T3 fibroblast (labelled in green), transfected with complementary DNA encoding PSR, extending a protrusion and engulfing a Jurkat T cell that has been induced to die by ultraviolet irradiation (labelled in red). Interestingly, the PSR gene is conserved in *Caenorhabditis elegans* and *Drosophila*, indicating that, as is the case for the apoptotic programme, the mechanisms of engulfment may be evolutionarily conserved.

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