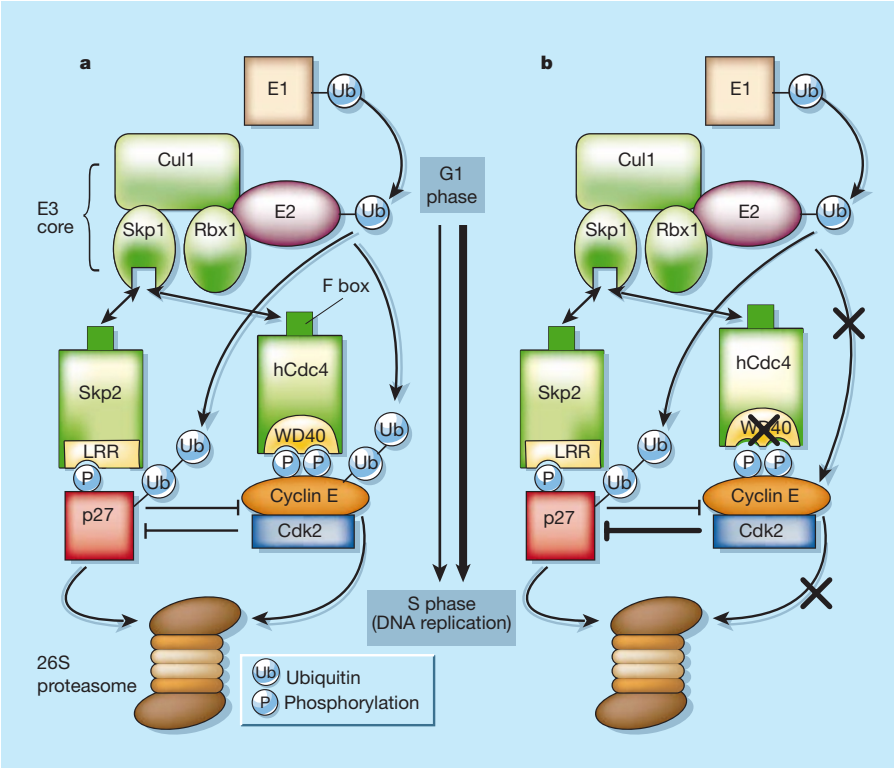

Figure 1 **Cell-cycle balancing acts. The enzyme Cdk2 is activated only at the transition from the G1 phase to the S phase of the cell cycle. This is achieved by a complex interplay between degradation of cyclin E, which is needed for Cdk2 to function, and of the Cdk2 inhibitor p27. Degradation occurs as follows. E1, E2 and E3 (green) enzymes add ubiquitin to substrate proteins, which are then directed to the 26S proteasome for destruction. New work[5–7] shows that hCdc4/Fbw7/Ago (shown as hCdc4) links phosphorylated cyclin E to a core E3 complex, termed SCF. Similarly, Skp2 recognizes phosphorylated p27 (ref. 16).** a, **In normal cells[1], growth factors stimulate the expression of both Skp2 and cyclin E, which cooperate to ensure the degradation of p27. With precise timing, the balance of activity is tipped in favour of cyclin E–Cdk2, which promotes S-phase entry.** b, **In tumour cells, mutation of Cdc4 prevents recognition of cyclin E, which is stabilized. This overwhelms p27, resulting in premature S-phase entry. WD40 and LRR are protein regions that recruit substrates for ubiquitination.**

and degradation, but only once the inhibitor has been phosphorylated by cyclin E–Cdk2 (ref. 16; Fig. 1). So cells lacking Skp2 would have excess p27, which would inhibit Cdk2 and prevent it from phosphorylating cyclin E. Cyclin E would not be recognized by hCdc4/Fbw7/Ago, and so would be stabilized. Alternatively, ubiquitination of cyclin E by Skp2 might require other unknown proteins that were not included in the *in vitro* experiments.

A second issue concerns the phosphorylation requirements for cyclin E recognition. In yeast, many substrates of Cdc4 must be phosphorylated on several sites before they can be recognized. Similarly, Strohmaier *et al.* find that the recognition of cyclin E depends on it being phosphorylated on at least two residues — threonines 62 and 380. This observation raises the possibility of several intriguing regulatory mechanisms, such as the existence of kinases in addition to Cdk2 that might target cyclin E for degradation. A detailed understanding of how hCdc4/Fbw7/Ago functions will be essential if the new results[5–7] are to be exploited in treating cancer and other diseases. ■

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Daedalus

Genomes and souls

The evolution of humanity is still a theological problem. Even the Catholic Church accepts evolution, but excludes the human soul from it. So, says Daedalus, presumably there was an advanced ape without a soul who gave birth to a baby that had one. Some mutation had created the human soul, our spiritual nature.

All the standard queries of evolution then cry out to be asked. If the soul is recessive, a creature with a soul mating with one with no soul would give soulless offspring. If it is dominant, the soul would spread rapidly, and (as claimed) all humanity would soon have souls. Furthermore, the argument implies that the soul is represented on the genome. One or more of the tens of thousands of genes in the human genome codes not for a protein, but for the soul.

Now that the human genome has been roughly described in its entirety, DREADCO biochemists are scanning it for a set of unusual bases conspicuously absent from the genomes of the higher animals. With luck they will identify such a set, associated with the soul. The way will then be open for several experiments, all highly controversial. First, this set of bases could be inserted in plasmid form into organisms too primitive to have much use for a soul, such as bacteria of the species *Escherichia coli*. Would they behave any differently from normal organisms of these species? Probably not; Daedalus reckons that a brain of some complexity is needed to support a soul. Either the transplant would fail, or the bases could not be switched on.

Alan Turing once suggested that a creature with a brain arguably capable of supporting a soul, such as an elephant, might be given one. In this case, new behaviour (such as praying) should certainly occur. Second, human beings deprived of the crucial bases, or perhaps with them 'switched off' by some binding ligand, should react in an inhumanly 'soulless' or destructive manner. But if the Lord objected to interference with His creation, the attempt to deprive humans of their souls would somehow fail.

And, of course, the genome occurs in every cell of the body. So transplant operations, in which organs are transferred from one person to another, would produce a chimaera with two souls, at least in theory. This suggests that the ultimate surgical operation, a brain transplant, will never work. It also suggests that no computer, however clever, can have a soul. David Jones