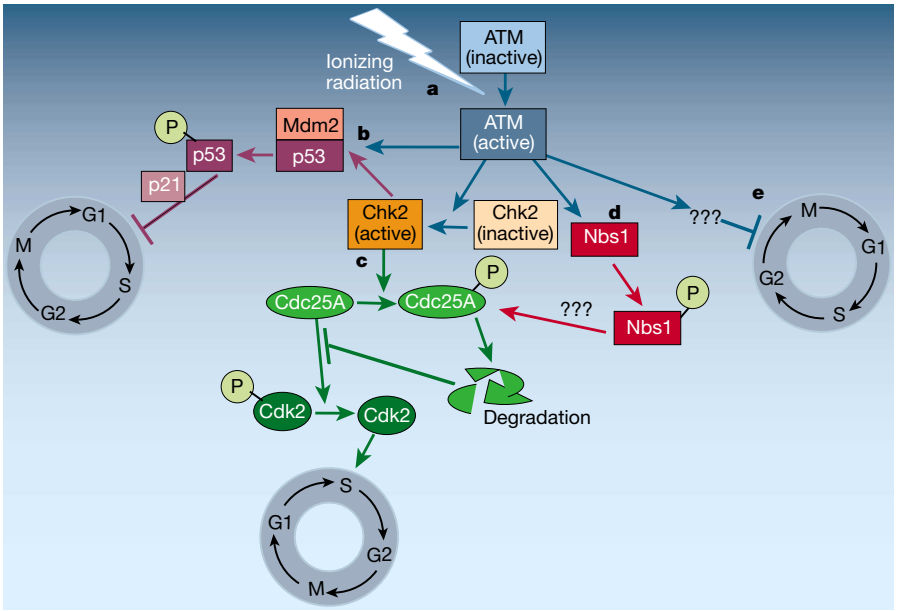

Figure 1 **Steps involved in the cell-cycle checkpoints that are induced in response to ionizing radiation. The pathway investigated by Falck *et al.*[3] is that shown in blue, orange and green.** a, **Ionizing radiation activates the kinase ATM, which in turn activates the kinase Chk2.** b, **This step appears to affect progression from G1 to the S phase, through phosphorylation (represented by a circled 'P') and stabilization of the p53 protein, which itself enhances the expression of the cell-cycle inhibitor p21.** c, **Activation of Chk2 by ATM also affects progression through the S phase itself, by the phosphorylation of Cdc25A. This protein is more likely to be degraded when phosphorylated. (When unphosphorylated, Cdc25A removes a phosphate group from Cdk2, enabling the initiation of DNA replication, that is, S phase.)** d, **Nbs1 is also phosphorylated by ATM and is also involved in the ionizing-radiation-induced inhibition of S-phase progression, although it is not known how it ties in to the pathway described by Falck *et al.*** e, **The targets of ATM that control progression from G2 into mitosis (M phase) have not been described.**

irradiation-induced signalling pathways and the cell-cycle machinery in the G1 phase was made with the discovery that the p53 protein (a target of Chk2 in the G1-checkpoint pathway) activates the expression of an inhibitor of the cell cycle, p21. Falck *et al.*'s experiments[3] linking ATM (which responds to ionizing radiation), through Chk2 and Cdc25A, to Cdk2 (which controls the cell cycle) appear to provide the same type of crucial link for S-phase progression.

But this won't be the end of the story. Other proteins will certainly be involved. For example, the protein Nbs1, which is also phosphorylated by ATM, is also required for this S-phase checkpoint[10,11]. It will be important to work out how this particular phosphorylation event is linked to those uncovered by Falck *et al.* In the ionizing-radiation-induced G1 checkpoint, ATM phosphorylates several proteins to accomplish its goal of halting the cell cycle[2]. Perhaps a similar scenario occurs during the control of the S-phase checkpoint (Fig. 1). It will also be important to determine whether inhibition of Cdk2 alone is sufficient to halt DNA replication, or whether other mechanisms are involved.

It is interesting that phosphorylation of Chk2 by ATM is required for both G1 and S-phase delays following ionizing radiation, even though Chk2 appears to work in different ways in the two pathways. (In the G1 arrest, Chk2 helps to prevent the degradation of one of its targets, p53; in the S-phase delay, Chk2 enhances the degradation of another target, Cdc25A.) ATM is also required for the G2-phase delay in response to ionizing radiation. If Chk2 turns out to be involved in this delay, too, then the differences between these three checkpoints would appear to lie downstream of ATM and Chk2. Finally, Falck *et al.*'s study serves as a model for investigations of how signal-transduction pathways (in this case, one induced by DNA damage) can be linked to their functional endpoint — here, control of the cell cycle. ■

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Daedalus

Flattening the flats

The art of making true optical flats — glass discs with surfaces polished so accurately that any unevenness is small compared with the wavelength of light —was revealed in the nineteenth century. (Until then, people had merely ground the weakest possible mirrors.) The trick is to grind three pieces of material against each other: A against B, B against C, and C against A. All three then become true flats — or at least as flat the distortion of the Earth's gravity permits. Lens telescopes have an advantage over mirrors in that a small sag in the lens makes essentially no difference to its optical performance. Daedalus has been musing on these facts because of the high value of true flats to astronomy. The accurate distance of many stars could be deduced if a space telescope, equipped with flats, could be used as an optical interferometer.

So Daedalus now shows how make true flats. The best Earthbound flats would be made by skilled opticians, and would be flown on the space shuttle. In microgravity it should be easy to complete the ultrafine grinding of the flats against each other, giving three flats of amazing performance.

Ideally, two of these flats should be attached to a space telescope, one in its light path and the other many kilometres away. The art of stabilizing an object in space has been perfected over many decades, and Daedalus hopes that the distant flat can be turned and held so as to shine the light of a distant star unwaveringly upon its fellow flat at the space telescope. The result should be an amazingly accurate interferometric measurement of the distance of the distant star.

Daedalus has no interest in the distance of stars per se. He wants to measure the distance of stars in nearby galaxies, and thus determine the Hubble constant with accuracy. It is rather shocking that this important constant seems to vary from 60 to 85 — and that astronomers can choose whichever value they like. They can also measure it in km s^{-1} Mpc^{-1}, instead of s^{-1} as the rest of us would have to, but that's another matter.

An accurate Hubble constant would allow cosmologists to say clearly if the Universe were 'open' (doomed to expand for ever) or 'closed' (due to fall back on itself as the galaxies do not quite have mutual escape velocity). Daedalus likes the idea of a closed Universe, in which the galaxies only just slow before falling back. But he recognizes that a Hubble constant accurately related to the time of the Big Bang will be needed to make it work. **David Jones**

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