between crustal thickness and the mean extent of melting inferred from the chemistry of erupted basalts[2] and residual peridotites[3], only the remaining, uncorrelated chemical variability can be attributed to the source.

This has led to the idea that variability along the mid-ocean-ridge system is mainly caused by temperature changes in the underlying mantle, which would affect the extent of melting of a reasonably homogeneous source. Such an idea is consistent with most (but not all) of the isotope data on the long-term history of the mantle sources of mid-ocean-ridge basalts. The zero-age view, however, gives little useful information about the geometry and dynamics of the flow of rock through the region of the mantle where melting occurs, or how this flow may vary with time.

This is where Bonatti and co-workers come in[1]. The exposure of the Vema transverse ridge (Fig. 1) has allowed them to dredge up and analyse rock that would normally be deeply buried. They have therefore been able to measure an apparent time-delay between changes in crustal thickness, as estimated from gravity data, and in residual peridotite chemistry over the 20-million-year timescale. Their chain of logic derives from the following observations. The signals indicating crustal thickness and the extent of peridotite depletion show oscillations that have a wavelength of about 60 km (corresponding to a 3–4-million-year frequency), superposed on an overall 20-million-year trend of increasing peridotite depletion and crustal thickness. The variations seen in the two signals are correlated, but there is a phase lag of 22 km (or some 1.3 million years of spreading time) between the signals.

Bonatti *et al.* attribute the overall 20-million-year thickening trend to long-term warming of the mantle beneath the equatorial Atlantic, caused by southwards flow of mantle from 'hotspots' in the North Atlantic (although they acknowledge that it could also be due to along-axis growth of this particular ridge segment with time). The most exciting aspect of this study, though, is the interpretation of the 3–4-million-year signal. Experts might ask for a tighter correlation between the time series of crustal thickness and extent of melting derived from peridotites, but this correlation seems to dispense with the need to invoke explanations for the observed variation in crustal thickness that depend entirely on melt migration or variation in the composition of the source rock.

That leaves variations in mantle temperature and flow geometry. There is no obvious reason why mantle temperature should oscillate at this 3–4-million-year frequency, but dynamical calculations, making certain assumptions about viscosity changes and the internal buoyancy of basalts and residual peridotites, predict that there would be bursts of increased flow through the melting region[4]. These episodes of rapid flow can explain times of high crustal thickness. But the mechanism by which they generate more depleted residual peridotites is unclear, as is the basis of the sawtoothed form of the crustal-thickness signal (as strikingly depicted in Fig. 3d on page 501). Bonatti *et al.* propose that the flow variation is restricted to the deeper, water-bearing, and hence low-viscosity, part of the melting regime[5] and that the intervals of active flow somehow deliver hotter material to the shallower, high-viscosity part of the melting regime. An alternative explanation is that the episodes of active flow change the balance between advection and conduction in the shallowest part of the melting region, as hinted at by equilibration temperatures that record different cooling rates in the same peridotites.

What of the 22-km offset between the signals denoting residual peridotite and crustal thickness? Melt migration is much more rapid than solid flow through the melting region, so there would be a time delay between melt extraction from a given parcel of peridotite to create basalts, and the eventual emplacement of that same peridotite as a residue at the base of the lithosphere. In other words, the oscillation signals carried by the melt volume and by peridotite chemistry propagate upwards at different speeds and are recorded at different times, being spatially offset by the plate spreading rate. Bonatti *et al.* use the phase lag between their extent-of-melting signals from peridotite and from crustal thickness (assuming that the bulk of the melt separates at a depth of 35 km and that melt velocity can be taken as infinite) to calculate the solid upwelling rate, and they arrive at an estimate of 25 mm per year. This is faster than the rate at which the plate is moving away from the ridge (14–17 mm per year) and hence is consistent with a component of buoyant flow.

Mid-ocean ridges have different characteristics according to their speed of spreading. At the Vema anomaly, the Mid-Atlantic Ridge is slow spreading, and Bonatti and colleagues' study adds to our understanding of how the oceanic crust grows in these circumstances. Similar understanding of fast-spreading sections, which do not tend to create such spectacular tectonic exposures, seems further away, but there is plenty more to learn from the Vema feature. For instance, it will be interesting to see whether informative chemical variations have been preserved in the basaltic rocks at the top of the section, and whether they correlate with the picture that Bonatti *et al.* have compiled from the data on crustal thickness and exposed mantle rocks. ■

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Cell division

Genome maintenance

Jordan W. Raff

Early fruitfly embryos have an unusual means of halting the division of any nuclei containing damaged DNA. A key component of this mechanism has now been identified, and might have implications for cancer.

Maintaining the integrity of the genome is a crucial task for any cell. Two proteins, called checkpoint kinases 1 (Chk1) and 2 (Chk2), help to achieve this in many species, and mutations in the genes encoding these proteins have been linked to the generation of cancer in humans. The proteins are activated by DNA damage, and help to initiate cellular defence responses that include the stimulation of DNA-repair pathways and the slowing down of the cell-division cycle to allow time for repair[1,2]. In multicellular organisms, if the DNA is not successfully mended, the damaged cells usually kill themselves — thereby eliminating the defective genome. As they describe in *Cell*, Theurkauf and colleagues[3] have discovered that Chk2 is also involved in a rather different defence mechanism that is triggered by DNA damage in early fruitfly embryos.

This particular defence response is especially well suited to the early fruitfly (*Drosophila*) embryo, in which the cell nuclei undergo a series of 13 rapid divisions within a common cytoplasm[4]. These swift nuclear divisions occur synchronously, and consist entirely of alternating phases of DNA synthesis (S phase) and DNA segregation (mitosis or M phase), with none of the intervening gap phases that separate S and M in more typical cell cycles. Because there is no gap

phase, if one of the embryonic nuclei is damaged during S phase, it does not have the usual option of stopping the division cycle before mitosis. Instead, it will be driven into mitosis, in synchrony with the surrounding undamaged nuclei in the common cytoplasm.

During nuclear-division cycles 9 and 10, most nuclei migrate to the outer rim of the embryo — the cortex (Fig. 1a). A few remain in the interior, but these will not contribute to the adult fly. It has been known for some time that, during cycles 10 to 13, any cortical nucleus that suffers DNA damage eventually drops into the interior of the embryo and is thereby effectively eliminated from the organism[5]. It has been a mystery, however, how such damaged nuclei are recognized and how they are then discharged into the interior.

Three years ago, Theurkauf and colleagues[6] described the phenomenon of centrosome inactivation in *Drosophila* embryos. Centrosomes are structures that are needed to efficiently segregate DNA during mitosis. They contain so-called γ-tubulin ring complexes (γ-TURCs), which organize the long filaments, or microtubules, that make up the mitotic spindle — a bipolar apparatus on which chromosomes are segregated. Theurkauf and co-workers[6] noticed that nuclei that failed to complete DNA synthesis or suffered DNA damage during S phase formed abnormal spindles when they entered mitosis. This was apparently because the DNA damage triggered the displacement of the γ-TURCs from the centrosomes during mitosis. Intriguingly, the γ-TURCs reappeared at centrosomes after mitosis was complete, and several other centrosomal proteins remained concentrated at centrosomes during mitosis, hinting that a core centrosome structure remained intact throughout the division cycle. The abnormal nuclei that reformed after the aberrant mitosis then rapidly dropped into the interior of the embryo, and so were effectively eliminated (Fig. 1b–d).

Theurkauf and colleagues[3] have now shown that double-stranded DNA breaks are responsible for triggering this centrosome inactivation, and that Chk2 is essential for the process. In vertebrate cells, many Chk2-dependent responses to DNA damage are induced via the activation of the p53 protein, but the authors found that this is not the case for centrosome inactivation. Moreover, they discovered that Chk2 itself becomes concentrated at centrosomes, and that DNA damage seems to enhance its accumulation there. So, given that Chk2 is a kinase — it modifies proteins by phosphorylating them — perhaps it inactivates centrosomes by directly phosphorylating one or more of their protein components.

Might Chk2 also induce centrosome inactivation in other cell types? As mentioned above, in most cells, DNA damage that occurs in the phases between mitoses (these phases are collectively known as interphase) causes a cell-cycle arrest prior to mitosis[1,2]. But this cannot occur in early *Drosophila* embryos, so a unique Chk2-dependent mechanism may have evolved to eliminate defective nuclei during mitosis instead. In support of this possibility, DNA damage in older, cellularized fruitfly embryos (when the nuclei no longer share a common cytoplasm, and there is a gap phase between S and M phases) does not appear to lead to centrosome inactivation, but instead causes a delay in both the entry into and exit from mitosis[7,8]. And in vertebrate cells in culture, DNA damage during mitosis does not induce centrosome inactivation[9] — although, even in early *Drosophila* embryos, DNA damage that occurs during mitosis does not appear to trigger centrosome inactivation, implying that Chk2 may need to be activated in interphase to cause centrosome inactivation in mitosis[3,6].

It seems unlikely, then, that centrosome inactivation is a major response to DNA damage in most normal cells, as DNA damage during interphase will usually lead to cell-cycle arrest before the cell enters mitosis. If, however, a cell manages to enter mitosis with unrepaired DNA damage, it might then become important to trigger centrosome inactivation in order to eliminate the defective DNA. In fact, there is some evidence that vertebrate cells that enter mitosis carrying damaged DNA die by a 'mitotic catastrophe'[10], although it is not clear whether this mechanism requires Chk2 or is indeed caused by centrosome inactivation. If such a process does exist, however, it might help to protect against cancer. The mechanisms that monitor DNA damage are often impaired in pre-cancerous cells, and so it may be relatively common for such cells to enter mitosis carrying defective DNA. If centrosome inactivation proves to be more than just a specialization of flies, the race will be on to understand how Chk2 brings it about, and to test whether it is involved in preventing human cancer. ■

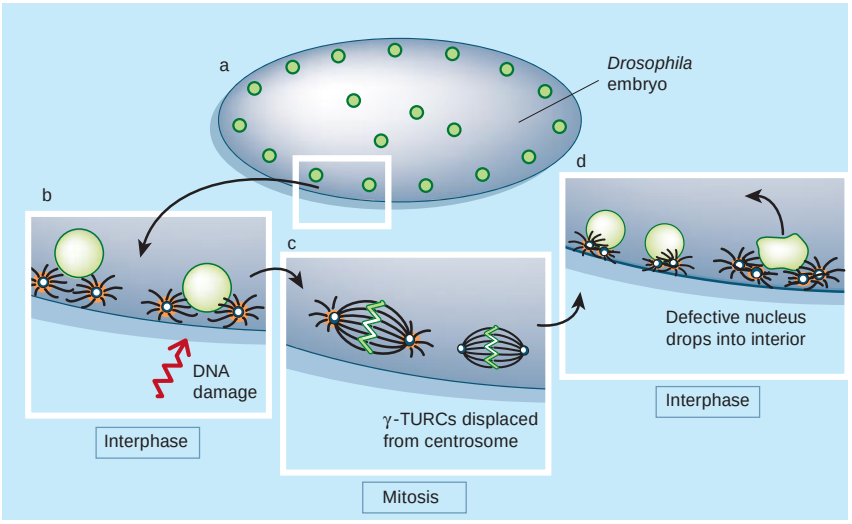

Figure 1 **Dealing with DNA damage in *Drosophila*.** a, **An early *Drosophila* embryo that has undergone 10–13 nuclear divisions. Most nuclei (green) are aligned around the outside, with only a few in the interior. These internal nuclei — 'yolk nuclei' — will not contribute to adult tissues.** b–d, **The fate of a nucleus whose DNA has been damaged in interphase (the period between one nuclear division and the next).** b, **At the time of DNA damage the centrosome is unaffected, and microtubules (black) are still organized by γ-tubulin ring complexes (γ-TURCs; orange) that are concentrated around a core centrosomal structure.** c, **As all the undamaged nuclei enter mitosis, so too does the damaged nucleus, but the γ-TURCs appear to be released from the centrosomes and the mitotic spindle (black) does not form properly. (Note that, at this point, the nuclear membrane has disintegrated, allowing the spindle to attach to chromosomes.) Chromosome segregation fails and, in the following interphase (**d**), the defective nucleus falls into the interior of the embryo, leaving the centrosomes behind. Theurkauf and colleagues[3] have found that the Chk2 protein is crucial for this nuclear defence mechanism.**

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