physiology. The importance of this protein for normal cell differentiation. Mutations in several genes that interact with transcription factors such as Ets, can also translocate to the nucleus, where it plays a role in the function of the cytoskeletal network. Actin- and membrane-associated proteins. But one member of the family, epiplakin, contains only plakin-repeat domains (PRD) - motifs that bind to assembled filaments (IFs). So what is its function? Shyh-Jeng Jang and co-workers have used RNAi and a new anti-epiplakin antibody to answer this question (p. 781). They show that epiplakin is closely associated with the keratin IF network in cells and preferentially interacts with assembled filaments rather than keratin monomers in vitro. They also demonstrate that knocking down epiplakin by RNAi causes a collapse of the IF network in simple epithelial cells - but, interestingly, not in epidermal cells. The authors propose that this member of the plakin family preserves the integrity of the IF network in these cells by bridging neighbouring IFs. They note that epiplakin levels in keratinocytes increase as the cells differentiate, suggesting this could be because new keratins (K1/K10) are expressed then.

Securin' a new role for separase
Separase is a protease that triggers separation of sister chromatids at mitosis by cleaving the cohesin complex that holds them together. In interphase, it is held in check by securin; this is then degraded at anaphase when separase activity is required. On p. 733, Christian Lehner and co-workers unveil additional roles for separase and securin in flies and cast doubt on previous suggestions (based on work in budding yeast) that they are required for completion of mitosis. The authors have used live-cell imaging of Drosophila embryos to investigate the effects of mutations in fly securin (PIM) and the separase regulatory subunit THR. Predictably, they observe that sister chromatids do not separate in pim and thr mutant epidermal cells. Nevertheless, these cells do exit mitosis and complete cytokinesis despite failing to segregate their DNA correctly. The most surprising finding, however, is that the mutants develop profound defects in epithelial tissue organization. Lehner and co-workers therefore conclude that separase regulates tissue integrity as well as genetic stability. Since separase has been shown to affect microtubule stability in yeast, it might control epithelial organization through such a mechanism.

Telomerase - a death-defying enzyme
The enzyme telomerase maintains telomere length by adding TTAGGG repeats to the ends of chromosomes when DNA replicates. Although highly expressed in stem cells, telomerase is hardly detectable in differentiated cells. It is reactivated during tumorigenesis, however, and appears to be associated with cell immortalization. Kanaga Sabapathy and co-workers now provide evidence that it also confers resistance to apoptosis (see p. 819). They have ectopically expressed the catalytic subunit of telomerase (TERT) in mouse embryonic stem (ES) cells. Significantly, this does not affect the ability of the cells to differentiate (which some previous results had suggested). But it does protect them against apoptosis that occurs during differentiation. Furthermore, the authors show that TERT confers resistance to apoptosis induced by oxidative stress and chemotherapeutic agents. They go on to demonstrate that it offers little protection against cell death in ES cells that lack the tumour suppressor p53, which is normally upregulated when these cells undergo apoptosis. Sabapathy and co-workers therefore conclude that telomerase provides resistance to p53-dependent apoptosis in ES cells. They also propose that it might thus represent a useful basis for improving the viability of stem cells for transplantation.

Development in press
An elusive companion for Hedgehog
Despite the remarkable conservation of the Hedgehog (Hh) signalling pathway through evolution, Costal2 (Cos2), a vital kinesin-related component of the pathway in flies, has previously escaped detection in vertebrates. In work published in Development, however, Tay et al. now report the identification of the first vertebrate homologue of Cos2, which they have cloned from zebrafish through its sequence similarity to fly Cos2. In knockdown experiments, the authors show that decreased Cos2 levels cause ectopic Hh signalling in zebrafish. This would be expected given its role in flies, in which Cos2 is thought to assemble a protein complex that ultimately leads to the Cubitus interruptus (Ci) mediated repression of Hh target genes. In vitro, zebrafish Cos2 can form a complex with Gli1, a homologue of Ci. Together with the mouse and human Cos2-like sequences also reported in the paper, these new findings provide important information about the mechanics of Hh signalling in vertebrates.