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STEM CELLS

Satellite cells shed light on asymmetrical DNA strand segregation

Most mutational changes in DNA are thought to result from replication errors during cell division. It has therefore been proposed that one way in which stem cells avoid accumulating mutations could involve asymmetrical DNA strand segregation during cell division — the stem cell would retain the template strand while its destined-to-differentiate daughter would receive the newly synthesized strand. Although conceptually appealing, this hypothesis has remained controversial, primarily owing to insufficient empirical evidence to support it. Recent work on mouse satellite cells — muscle-cells with adult stem cell properties — shows that, as in other systems, the template DNA strand does not segregate randomly after mitosis and the template strand cosegregates with Numb, an asymmetrical cell-fate determinant which is a read-out of asymmetrical cell divisions.

Satellite cells give rise to myoblasts during postnatal development and after injury. To better understand the stem-cell-like properties of these cells Shinin *et al.* studied one mechanism of stem cell renewal — asymmetrical cell division. The authors showed that cultured mouse satellite cells indeed divide asymmetrically, well before differentiation, as determined by the asymmetrical segregation of Numb-GFP. Moreover, based on the fate of centrosomes after mitosis, the authors suggest that Numb is most probably associated with the self-renewal fate.

Stem cells and their niches have been identified in a number of tissues by pulse-chase experiments; this approach is possible because slowly dividing cells retain nucleotide analogues that mark DNA for longer than their faster dividing neighbours. The authors used the same approach to confirm that satellite cells represent the stem cell compartment within a muscle fibre. To examine the clonogenicity potential of the label-retaining cells, Shinin *et al.* established clones from satellite cells isolated from BrdU pulse-chased mice. They noticed that although most clones diluted the label as the cells proliferated, in some cases individual cells retained the label while their neighbours were label-free. Given that the label-free cells continue to divide, these observations were consistent with the retention of the template strand by stem cells, as postulated by John Cairns some 30 years ago (see Further reading). By directly observing individual labelled satellite cells using videomicroscopy and further *in vitro* and *in vivo* analysis Shinin *et al.* confirmed that, as had been shown in epithelial and neuronal stem cells, asymmetrical segregation of template DNA strands also occurs in satellite cells.

Could the asymmetrical segregation of template DNA and Numb in satellite cells be related? Indeed, in 90% of cells that show asymmetry of both events, the template DNA and Numb end up in the same daughter cell. Given that Numb is considered as a read-out of the cell asymmetry apparatus, the authors' results provide a link between it and the asymmetrical segregation of template DNA. Further experiments will be needed to investigate the nature of this link and the mechanism of template DNA strand cosegregation.

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ORIGINAL RESEARCH PAPER Shinin, V. *et al.* Asymmetric division and cosegregation of template DNA strands in adult muscle satellite cells. *Nature Cell Biol.* 25 June 2006 (doi:10.1038/ncb1425)

FURTHER READING Cairns, J. Mutation selection and the natural history of cancer. *Nature* **255**, 197–200 (1975)