TELOMERES

More than just the 'maintenance man'

In higher organisms, the proliferative and multipotent properties of adult stem cells enable the maintenance and regeneration of different tissues. These stem cells express high levels of telomerase, which is the ribonucleoprotein enzyme that extends telomeres during DNA duplication. As telomeres must be sufficiently long for cell division to take place, the increased activity of telomerase is probably one of the factors that endow these cells with their large proliferative capacity.

But does telomerase have other roles in the stem-cell compartment apart from the maintenance of chromosome ends? A group of scientists led by María Blasco at the Spanish National Cancer Center tackled this question by analysing the behaviour of epidermal stem cells in mouse models of defective telomerase expression.

The authors showed that, in G1 telomerase deficient ($Terc^{-/-}$) mice, in which telomeres are only slightly reduced in length, and in G3 $Terc^{-/-}$ mice, which have critically short telomeres, epidermal stem cells accumulated in their niche in the bulge of the hair follicle. Cells from both G1 and G3 mice were unable to mobilize efficiently from the bulge and did not initiate appropriate hair growth in response to a proliferative stimulus. Also, the *in vitro* proliferative capacity of epidermal stem cells derived from both G1 and G3 $Terc^{-/-}$ mice was impaired.

By contrast, in K5-*mTert* mice, in which epidermal stem cells overexpress the protein component of telomerase, the hair follicle niche was depleted of stem cells and, compared to wild-type mice, an increased proportion of these cells was mobilized by a proliferative stimulus. These cells also showed a markedly increased capacity to proliferate *in vitro*.

Taken together, these results indicate that the role of telomerase is not merely to maintain chromosome ends — telomerase activity *per se* has a crucial role in regulating stem-cell turnover and mobilization. As $Terc^{-/-}$ mice have an ageing-resistant phenotype, and K5-*mTert* mice have a propensity to develop skin tumours, these effects of telomerase on stem-cell behaviour are crucial in the aetiology of both cancer and ageing.

Shannon Amoils

References and links

ORIGINAL RESEARCH PAPER Flores, I., Cayuela, M. L. & Blasco, M. A. Effects of telomerase and telomere length on epidermal stem cell behavior. *Science* 21 July 2005 (doi:10.1126/science.1115025)

IN BRIEF

SIGNAL TRANSDUCTION

Genome-wide RNAi analysis of JAK/STAT signaling components in *Drosophila*.

Baeg, G.-H., Zhou, R. & Perrimon, N. *Genes Dev.* 29 July 2005 (doi:10.1101/gad.1320705)

An RNA interference (RNAi) screen in *Drosophila melanogaster* cells uncovered new regulators of the Janus kinase (JAK)–signal transducer and activator of transcription (STAT) pathway. Some genes were required for tyrosine phosphorylation of STAT92E. Others (homologues of mammalian RanBP3 and RanBP10) regulated its nucleoplasmic shuttling. The protein tyrosine phosphatase PTP61F was identified as a JAK–STAT-induced transcriptional target that functions in a negative-feedback loop.

TRAFFICKING

Depalmitoylated Ras traffics to and from the Golgi complex via a nonvesicular pathway.

Goodwin, J. S. *et al. J. Cell Biol.* **170**, 261–272 (2005)

Goodwin *et al.* studied how palmitoylation affects the trafficking and subcellular localization of H- and N-Ras and present a model in which both isoforms are kinetically 'trapped' on Golgi membranes by palmitoylation before moving to the cell surface in vesicles. Here, depalmitoylation facilitates Ras release. The isoforms then return by a non-vesicular pathway to the Golgi, where they are repalmitoylated, and so rejoin the vesicular transport pathway.

DNA REPAIR

Dynamic assembly and sustained retention of 53BP1 at the sites of DNA damage are controlled by Mdc1/NFBD1.

Bekker-Jensen, S. *et al. J. Cell Biol.* **170**, 201–211 (2005)

The checkpoint mediator 53BP1 accumulates at double-strand DNA breaks (DSBs), but how does it interact with them? Bekker-Jensen *et al.* showed in live mammalian cells that an interaction between 53BP1 and chromatin increases at DSB sites. This is strengthened by another DSB-interacting checkpoint mediator, MDC1/NFBD1, which is assembled at DSBs before 53BP1 is. MDC1/NFBD1 is proposed to 'bridge' damaged chromatin that is marked by Ser139-phosphorylated histone H2AX with 53BP1.

CELL DIVISION

Asymmetric cell divisions promote stratification and differentiation of mammalian skin.

Lechler, T. & Fuchs, E. *Nature* 10 Aug 2005 (doi:10.1038/nature03922)

Epidermal stratification is thought to occur by delamination and subsequent upward movement of epidermal cells. Lechler and Fuchs provide evidence for an alternative mechanism — asymmetric cell division. In embryonic mouse skin, >70% of mitotic spindles were aligned perpendicularly to the basement membrane as a result of the apical localization in mitotic basal cells of atypical protein kinase C, an LGN–PAR3–Inscuteable complex and a NuMA–dynactin complex. Asymmetric cell division then yielded one proliferative basal and one committed suprabasal cell concomitant with the occurrence of stratification.