with a previous claim that the first cloned sheep, Dolly, had shorter telomeres than control animals of the same age. Evidently, cellular senescence also correlates with telomere shortening in animals cloned by NT. Indeed, the rate of telomere erosion might determine the lifespan of both donor and cloned sheep fibroblasts.

The authors conclude that proliferative capacity and rates of telomere erosion are conserved during nuclear transfer, and are therefore likely to be a genetically determined property in sheep. A crucial question that remains unanswered is whether there is any effect on overall organismal ageing or pathologies such as cancer. How and if replicative senescence and telomere biology are related to ageing remains an important frontier for future investigation.

Bernd Pulverer, Editor,
Nature Cell Biology

References and links

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GENE REGULATION

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The worm is no longer the 'odd one out' when it comes to the involvement of Polycomb-like proteins in the maintenance of Hox gene repression, thanks to the work of two groups who report their findings in the June issue of *Developmental Cell*. Although this regulation has been known for years in *Drosophila* and mammals, up until now there has been no evidence for it in *Caenorhabditis elegans*. Previously, worm genes that encode the ESC-E(Z) Polycomb group (PcG) complex were thought to function solely in germline development.

In *C. elegans*, as in other animals, Hox genes pattern the anterior–posterior (A/P) axis. The male worm tail produces sensory rays that adopt characteristic morphologies along the A/P axis, and so rays provide a useful readout of defects in Hox gene expression. Both groups carried out suppressor mutagenesis screens on ray-defective mutants to identify potential repressors of Hox gene expression.

In the process of looking for suppressors of ray defects, Ross and Zarkower isolated *mes-3*, which is known to function in a complex with the worm PcG proteins, *mes-2* (the ESC orthologue) and *mes-6* (the E(Z) orthologue), during germline development. When the authors investigated single mutants of all three genes they found weak defects in ray patterning and ectopic Hox gene expression along the whole body axis. So, in the worm soma, as in mammals and the fly, PcG proteins negatively regulate Hox gene expression.

How do these *mes* genes control Hox expression? A clue comes from the fact that RNAi targeted against certain histone deacetylases mildly phenocopies the *mes* mutants. Therefore, PcG proteins in worms might affect gene expression through histone modification, as they do in other species.

Zhang and colleagues give a different insight into Hox regulation in worms, from their study of the *sop-2* mutant. This mutant was previously isolated in a suppressor screen on *pal-1* mutants, which have incorrectly patterned sensory rays. Similar to the *mes* worms, *sop-2* mutants ectopically express Hox genes and produce extra rays. SOP-2 is a novel protein, but it does contain a self-associating SAM domain that is also found in certain PcG proteins. So, this provides another link between PcG-like genes and Hox regulation. In flies and mammals there are two distinct Polycomb group complexes, ESC-E(Z) and PRC. Worms do not have genes encoding the latter complex, and therefore it is possible that SOP-2 fulfils its functions.

These studies provide convincing evidence that *C. elegans* and all other metazoan phyla maintain correct Hox gene expression patterns through PcG-like regulation, but both papers raise questions. For instance, why are the somatic phenotypes of the worm *mes* mutants so subtle, when PcG mutations in *Drosophila* are severe? Another intriguing finding is that at the sequence level, *sop-2* is more related to the ETS family of transcription factors than Polycomb proteins. This indicates that *sop-2* is not merely a highly diverged PcG protein. But it remains to be seen how, when and why this gene evolved a function in chromatin regulation and to what extent SOP-2 replaced the functions of the PRC complex.

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WEB SITES

Zarkower's laboratory: http://www.cbc.umn.edu/~zarkoweb
Emmon's laboratory: http://worms.aecom.yu.edu/index.html