

## AGEING

## Recapturing youth

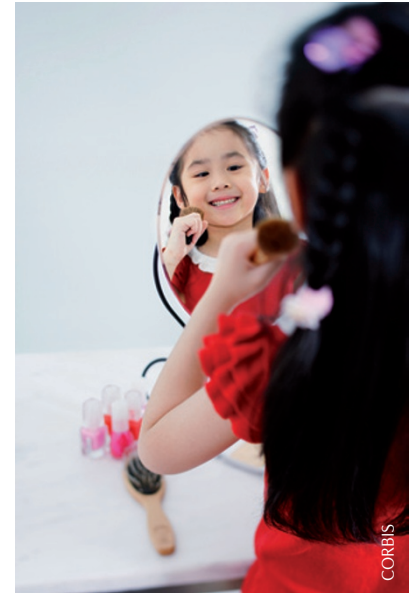
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The detrimental traits associated with the ageing of eukaryotes are not passed on to progeny, but how replicative lifespan (RLS; that is, the number of buds a cell can produce) is reset in the next generation is unknown. Amon and colleagues proposed that RLS is reset during gametogenesis (sporulation) in the budding yeast *Saccharomyces cerevisiae*, and they then showed that this is indeed the case.

In yeast, gametogenesis requires meiosis, in which two rounds of chromosome segregation result in the formation of a tetrad of haploid spores. The authors first induced the sporulation of young and aged *S. cerevisiae* cells, observing that the RLS of the spores produced by cells of both ages was the same. They next assessed how sporulation influences specific age-related cellular events, including protein aggregation (protein aggregates associated with heat shock protein 104 (Hsp104) can be seen as foci when Hsp104 is visualized), aberrant nucleolar structures and an increase in extrachromosomal ribosomal DNA circles (ERCs). Although foci of Hsp104 tagged with enhanced green fluorescent protein (Hsp104-EGFP) were observed in aged cells during sporulation, they were absent from the resulting tetrad of spores. Furthermore, ERCs decreased during sporulation in

ageing cells to a level similar to that in young cells and, although aged cells contained aberrant nucleolar structures, most of the tetrads they produced did not. Thus, sporulation seems to reset RLS in budding yeast by removing age-induced cellular features.

But exactly which stages of gametogenesis are required to reset RLS? Sporulating budding yeast cells can resume vegetative growth when the sporulation cue (nutrient deprivation) is withdrawn. This enabled the authors to assess whether RLS is reset in aged cells in which sporulation has been induced but blocked at a specific stage. Cells in which meiosis-inducing 1 (*IME1*; the protein product of which is required to initiate sporulation) was deleted did not reset RLS. Furthermore, Ndt80, a transcription factor that is required for cells to exit the pachytene phase of meiosis I, was also needed. Thus, *Ime1*-induced sporulation and Ndt80-induced processes are required to reset RLS. Interestingly, although the requirement of Ndt80 indicates that later stages of sporulation might be important for resetting RLS, the authors found that RLS is reset in cells that are prevented from completing even the first meiotic division. Thus, meiotic divisions themselves are not required to reset RLS.



Finally, the authors asked whether Ndt80 could extend the RLS of vegetative cells. Transient expression of Ndt80 expanded RLS of both aged and young cells. Importantly, Hsp104-EGFP foci and ERCs were not reduced by Ndt80 expression, but the number of cells with enlarged nucleoli was. Thus, it seems that to reset RLS Ndt80 must restore nucleolar morphology to that seen in young cells. As the authors point out, it will be interesting to determine whether ageing is also reset during gametogenesis in other species.

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**ORIGINAL RESEARCH PAPER** Ünal, E., Kinde, B. & Amon, A. Gametogenesis eliminates age-induced cellular damage and resets life span in yeast. *Science* **332**, 1554–1557 (2011)