File S2

Supporting Text

Calculation of the ratio of tetrads displaying different senescence for their telomerase-deficient spores to the total number of tetrads.

We made the assumption that telomeres are independently regulated regarding their length, as suggested in figure 1*D* where two telomeres in different clones did not show correlated lengths and in (Shampay and Blackburn 1988). We considered a *TLC1/tlc1Δ* diploid cell with 64 independent telomeres. Let us order these 64 telomeres by their length: $L_1 \leq L_2 \leq \ldots \leq L_{64}$, corresponding to the telomeres T_1, T_2, …, T_{64}, respectively. At prophase I of meiosis, all 64 telomeres are replicated. For a given telomere T_n ($1 \leq n \leq 64$), we assumed that the length of the two replicated strands was the same: if we called the two telomeres T_n and T_n', we assumed that $L_n = L_n'$ ($1 \leq n \leq 64$). In theory, there should be a difference of about the overhang length (~10 nt) between L_n and L_n'. As shown in figure 5*A*, however, this difference has no phenotypic consequence in the senescence onset, as mother and daughter cells always displayed similar senescence, even though mitotic replication should generate the same difference in length for a given telomere. Therefore, this assumption seems valid considering the sensitivity of the spot assay.

Meiotic crossing-overs would exchange telomeres between homologous chromosomes with the highest ratio as telomeres are located at the ends of chromosomes. Thus, meiosis randomly divides out these 128 telomeres (T_1, T_1', T_2, T_2', …, T_{64}, T_{64}') between the four spores.

First hypothesis: the senescence signal is controlled by a dominant telomere, likely the shortest.

Let us analyze how telomeres T_1 and T_1' segregate between the four spores. There are 12 possibilities (see below for the complete list). In two cases, both T_1 and T_1' fall into the two *tlc1Δ* spores (either T_1 into spore 1 and T_1' into spore 2, or the reverse). Thus, there is a 1/6 probability that T_1 and T_1' fall into the two *tlc1Δ* spores. Similarly, there is also a 1/6 probability that T_1 and T_1' fall into the two *TLC1* spores. That leaves a 2/3 probability that T_1 falls into a *tlc1Δ* spore and T_1' falls into a *TLC1* spore, or the reverse[*].

Under the hypothesis that a dominant telomere, likely the shortest shortest controls the senescence signal, there should be, for the two *tlc1Δ* spores:

1- No difference in senescence if both T_1 and T_1' fall into the two *tlc1Δ* spores (P = 1/6)

[*] The same result could be obtained by classical tetrad analysis where 1/6 are ditype parental (for instance, T_1 and T_1' in the two *tlc1Δ*), 1/6 ditype non-parental (T_1 and T_1' in the two *TLC1*) and 2/3 are tetratypes.

2- Differential senescence if either T_1 or T_1' falls into a *tlc1Δ* spore but not the other (P = 2/3)

3- Unknown result if both T_1 and T_1' fall into the two *TLC1* spores (P = 1/6), because senescence onset should then be controlled by T_2 and T_2'. We can then apply the same reasoning to T_2 and T_2' and show that with a 1/6 probability, the two *tlc1Δ* spores should display the same senescence onset; with a 2/3 probability, different senescence onsets; and with a 1/6 probability, a result that would depend on T_3 and T_3'.

Therefore, we recursively show that the two *tlc1Δ* spores should have the same senescence onset with the following probability:

$$P = 1/6 + (1/6)^2 + \ldots + (1/6)^{32} \approx 1/5 = 20\%$$

And the two *tlc1Δ* spores should display differential senescence with the complementary probability:

$$1 - P \approx 80\%$$

Second hypothesis: the senescent cell is not able to detect the shortest telomere.

In this case, a minimal postulate would be that the senescent cell cannot distinguish between the shortest and the second shortest telomeres, which is equivalent, for calculation simplicity, to $L_1 = L_2$ while keeping control by the shortest telomere as an assumption. Other postulates would lead to an even lower probability of different senescence onsets for the two *tlc1Δ* spores. This case is best illustrated by a two-way table with all 12 possible segregations of T_1/T_1' into the four spores along one dimension and all 12 possible segregations of T_2/T_2' on the other. The output in each square will be "=", meaning "same senescence onset for the two *tlc1Δ* spores", if the two *tlc1Δ* spores have either one of the four T_1, T_1', T_2, or T_2'; "≠", meaning "different senescence onsets for the two *tlc1Δ* spores", if one has T_1, T_1', T_2, or T_2' but the other none of these telomeres; or "?" if these four telomeres fall into the two *TLC1* spores.

The 12 possibilities for segregation are listed below:

	*tlc1*Δ #1	*tlc1*Δ #2	*TLC1* #1	*TLC1* #2
1	T	T'		
2	T'	T		
3	T		T'	
4	T			T'
5		T	T'	
6		T		T'
7	T'		T	
8	T'			T
9		T'	T	
10		T'		T
11			T	T'
12			T'	T

The rules we stated above lead to the following two-way table:

$T_2 \backslash T_1$	1	2	3	4	5	6	7	8	9	10	11	12
1	=	=	=	=	=	=	=	=	=	=	=	=
2	=	=	=	=	=	=	=	=	=	=	=	=
3	=	=	≠	≠	=	=	≠	≠	=	=	≠	≠
4	=	=	≠	≠	=	=	≠	≠	=	=	≠	≠
5	=	=	=	=	≠	≠	=	=	≠	≠	≠	≠
6	=	=	=	=	≠	≠	=	=	≠	≠	≠	≠
7	=	=	≠	≠	=	=	≠	≠	=	=	≠	≠
8	=	=	≠	≠	=	=	≠	≠	=	=	≠	≠
9	=	=	=	=	≠	≠	=	=	≠	≠	≠	≠
10	=	=	=	=	≠	≠	=	=	≠	≠	≠	≠
11	=	=	≠	≠	≠	≠	≠	≠	≠	≠	?	?
12	=	=	≠	≠	≠	≠	≠	≠	≠	≠	?	?

In these 144 squares, if we neglect the four "?" squares, we obtain the following probability of getting two *tlc1Δ* spores with the same senescence onset:

$$P \approx 76/140 \approx 54\%$$

And the probability for the two *tlc1Δ* spores to display different senescence onset would be:

$$1 - P \approx 46\%$$

We can notice that this calculation is also valid if the phenotypic assay, namely the spot assay, is not sensitive enough to distinguish between senescence onsets induced by the difference in length between T_1 and T_2. This might explain why there was a slight difference between our experimental 71% ratio and the theoretical 80% ratio.

Lastly, we also considered the uninvestigated possibility that telomerase may act at prophase I of meiosis before division on T_1 but not T_1' (or the reverse). Given the range of length of T_1 and T_1' in our simulations (around 180–200 bp), the probability of extension by telomerase is around 15% (Fig. S1*A*). This would generate a difference in length between T_1 and T_1' if telomerase acts on one but not the other, which corresponds to a probability of 0.15 × (1-0.15) = 0.1275. This has to be applied to all cases where we are supposed to observe a similar senescence for the two telomerase-deficient spores because they received T_1 and T_1'. Such cases amount to 2 out of the 12 possibilities in the previous table. Thus, these 2/12 ≈ 17% have to be corrected down by the 0.1275 probability of extension, which leads to 0.1275 × 2/12 ≈ 0.02. Overall, if we consider that telomerase can differentially act at prophase I on two sister chromatid telomeres, this would theoretically change the ratio of tetrads with similar senescence for the two telomerase-deficient spores from 20% to ~18%, and the ratio of tetrads with different senescence onsets for the two telomerase-deficient spores from 80% to ~82%.

SI REFERENCE

Shampay, J., and E. H. Blackburn, 1988 Generation of telomere-length heterogeneity in Saccharomyces cerevisiae. Proc Natl Acad Sci U S A 85**:** 534-538.