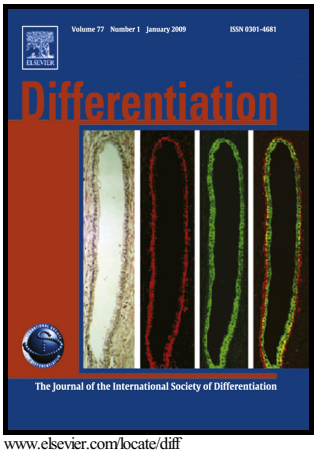
# Increased TERRA levels and RNase H sensitivity are conserved hallmarks of post-senescent survivors in budding yeast

Stefano Misino, Diego Bonetti, Sarah Luke-Glaser, Brian Luke




www.elsevier.com/locate/diff

PII: S0301-4681(17)30149-4
DOI: https://doi.org/10.1016/j.diff.2018.02.002
Reference: DIFF526

To appear in: *Differentiation*

Received date: 15 November 2017
Revised date: 8 February 2018
Accepted date: 14 February 2018

Cite this article as: Stefano Misino, Diego Bonetti, Sarah Luke-Glaser and Brian Luke, Increased TERRA levels and RNase H sensitivity are conserved hallmarks of post-senescent survivors in budding yeast, *Differentiation,* https://doi.org/10.1016/j.diff.2018.02.002

# Increased TERRA levels and RNase H sensitivity are conserved hallmarks of post-senescent survivors in budding yeast

Stefano Misino[1], Diego Bonetti[2,3], Sarah Luke-Glaser[2,*], Brian Luke[1,2,*]

[1]Institute of Neurobiology and Developmental Biology, JGU Mainz, Ackermannweg 4, 55128 Mainz, Germany

[2]Institute of Molecular Biology (IMB), Ackermannweg 4, 55128 Mainz, Germany

[3]Current address: Dipartimento di Biotecnologie e Bioscienze; Università degli Studi di Milano Bicocca; Milano, 20126; Italy

b.luke@imb-mainz.de

s.luke-glaser@imb-mainz.de

*Correspondence should be addressed to.



## ABSTRACT

Cancer cells activate telomere maintenance mechanisms (TMMs) to bypass replicative senescence and achieve immortality by either upregulating telomerase or promoting homology-directed repair (HDR) at chromosome ends to maintain telomere length, the latter being referred to as ALT (Alternative Lengthening of Telomeres). In yeast telomerase mutants, the HDR-based repair of telomeres leads to the generation of 'survivors' that escape senescence and divide indefinitely. So far, yeast has proven to provide an accurate model to study the generation and maintenance of telomeres via HDR. Recently, it has been established that up-regulation of the lncRNA, TERRA (telomeric repeat-containing RNA), is a novel hallmark of ALT cells. Moreover, RNA-DNA hybrids are thought to trigger HDR at telomeres in ALT cells to maintain telomere length and function. Here we show that, also in established yeast type II survivors, TERRA levels are increased in an analogous-manner to human ALT cells. The elevated TERRA levels are independent of yeast-specific subtelomeric structures, i.e. the presence or absence of Y' repetitive elements. Furthermore, we show that RNase H1 overexpression, which degrades the RNA moiety in RNA-DNA hybrids, impairs the growth of yeast survivors. We suggest that even in terms of TERRA regulation, yeast survivors serve as an accurate model that recapitulates many key features of human ALT cells.