

The CST complex is a terminator of telomerase activity

## ACCORCIAMENTO DEL TELOMERO

# TZAP: A telomere-associated protein involved in telomere length control

Julia Su Zhou Li et al 2017 Science

TZAP (telomeric zinc finger-associated protein).

TZAP binds preferentially to long telomeres that have a low concentration of shelterin complex, competing with the telomeric-repeat binding factors TRF1 and TRF2.

TZAP triggers telomere trimming, which results in the rapid deletion of telomeric repeats.

The reduced concentration of the shelterin complex at long telomeres results in TZAP binding and initiation of telomere trimming. Binding of TZAP to long telomeres represents the switch that triggers telomere trimming, setting the upper limit of telomere length.



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MAAAS

Chromatin immunoprecipitation (ChIP) shows association of TRF1 and TZAP to telomeric DNA



Bars represent the fraction of sequences containing four telomere repeats from the total reads obtained by ChIP-seq analysis

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#### Fig. 2 The zinc finger domains of TZAP directly bind telomeric repeats.



constructs used to show that the zinc finger domains of TZAP are sufficient for telomeric localization.







constructs in TRF2-null MEFs



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Fig. 2 The **terminal** zinc finger domains of TZAP directly bind telomeric repeats.









doxycycline-inducible expression of FLAG-TZAP at telomeres with and without MYC-TRF2 overexpression.

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Telomere restriction fragment analysis of cells at the indicated time points after infection (days).





Metaphase spreads of U2OS cells infected with the indicated constructs, analyzed by FISH. Telomeric DNA probe, green

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#### TTAGGGGTTAGG

AATCCCAATCCCAATCCCAATCCCAATCCCAATCCCAATC-5'



Telomere trimming involves the deletion of the secondary telomeric structures known as T-loops, leading to telomere shortening and accumulation of extrachromosomal telomeric DNA (ECT-DNA)



C-circle analysis to detect extra chromosomal telomeric DNA (ECT-DNA) in cells expressing the indicated constructs 6 days after infection.

single-stranded C-circle assay





Two-dimensional electrophoresis to detect ECT-DNA in U2OS cells 6 days after infection.

Gels were denatured and probed with a telomeric probe; arrows indicate circular telomeric species

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Q-FISH analysis of mouse embryonic stem (mES) cells either with lentiviral infection of TZAP or without



#### **Telomere length regulation**



