

# ANALYSIS OF TELOMERE CONSTELLATIONS AND DYNAMICS. RELATION TO CELL CYCLE AND HEALTH STATUS.

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Telomeres are considered to play an important role in spatial genome organization. On one hand these highly repetitive sequences are found anchored to a nuclear scaffold [1]; on the other hand not all telomeres appear to be attached at the same time, rendering some telomeres more mobile. Indeed, dynamic telomeres and telomere collisions have been reported [2]. Transient associations might reflect transcriptional and/or recombinational processes. Alongside these transient associations, telomeres show more permanent tethering, ranging from pairs in normal cells to large dysfunctional aggregates heralding chromosomal instability or apoptosis [3,4]. To study telomere patterns and mobility quantitatively in stable and transient transfectants, we combine 4D microscopy with dedicated image analysis tools. The number of telomeres detected is far below the expected number – about half on average – making tethering likely in mortal as well as immortal cell types. Unlike yeast, where a small number of telomeric clusters tether to the nuclear envelope, all mammalian cell types examined, show a broad, but non-random distribution pattern throughout the nuclear volume, with a preference for the more central part of the interphase nucleus. Moreover, we found that human telomeres replicate throughout S-phase, with over 50% of the telomeres replicating in mid-S-phase. Time lapse experiments reveal that relative telomere mobility is low; with on average a velocity of 0.40 $\mu$ m/min with a maximum of 1.33 $\mu$ m/min. The average radius of constraint was 0.74 $\mu$ m. As MSD-plots flatten over longer time periods, we conclude that telomeres undergo a constrained diffusive motion which supports the idea of (at least temporal) confinement/anchoring. We are now further characterizing the role of telomere based architecture, by studying possible interactions with other architectural elements (e.g. lamins) and its reorganization after physical, chemical or biological stress.

## References

- [1] T. de Lange, “Human telomeres are attached to the nuclear matrix”, *EMBO J.*, **11(2)**, 717-724 (1992).
- [2] C. Molenaar et al., “Visualizing telomere dynamics in living mammalian cells using PNA probes”, *EMBO J.*, **22(24)**, 6631-6641 (2003).
- [3] S. Louis et al., “c-Myc induces chromosomal rearrangements through telomere and chromosome remodeling in the interphase nucleus”, *PNAS*, **102(27)**, 9613-9618 (2005).
- [4] V. Raz et al., “Changes in lamina structure are followed by spatial reorganization of heterochromatic regions in caspase-8-activated human mesenchymal stem cells”, *J. Cell Sci.*, **119**, 4247-4256 (2006).