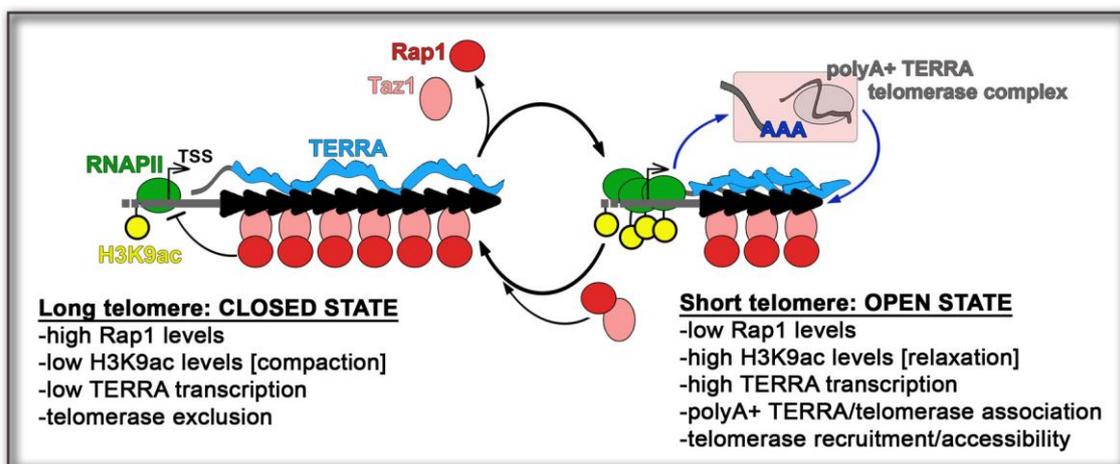


Title: Understanding the roles of the long noncoding RNA TERRA in telomerase-mediated telomere elongation in human cancer cells

Synopsis:

Cancer cells need to maintain the ends of their chromosomes, the telomeres, in order to achieve immortality. 85% of human cancers have reactivated a specialized reverse transcriptase dubbed telomerase, which is able to synthesize new telomeric repeats and add them to the very end of chromosomes. While the biochemistry of the telomerase reaction is fairly well established, the mechanistic bases of telomerase activity in cells remain to be elucidated. In particular, while it has been shown that telomerase is able to specifically recognize and elongate the shortest telomeres in cells, it is unknown how this recognition step is executed. Using the fission yeast *Schizosaccharomyces pombe* as a model system, we recently discovered that the long noncoding RNA TERRA ('telomeric repeat-containing RNA') is preferentially transcribed from short telomeres and that it physically interacts with telomerase. We also showed that experimentally induced transcription of a telomere promotes its association with telomerase and thus elongation. We intend to test a model where TERRA and/or telomere transcription specifically 'label' the shortest telomeres in human cancer cells in order to target them to telomerase-mediated telomere elongation. To this goal, we will apply molecular biology, cell biology and high end microscopy of both live and fixed cells to different human cultured cancer cells where transcription and length of specific telomeres will be manipulated using *in vivo* expression of DNA endonucleases and the CRISPR/Cas9 technology. This research project should not only contribute to expand our understanding of telomerase biology, but also unveil possible novel molecular targets for cancer therapy.



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Remunerated or volunteer training: volunteer.