

CNIO RESEARCHERS IDENTIFY A SET OF PROTEINS WHICH BIND TO TELOMERIC RNAs (TERRA) REGULATING THEIR FUNCTIONS

Madrid, June 29th, 2010 - Researchers from the Telomere and Telomerase Group of the Spanish National Cancer Research Centre (CNIO) have identified a set of RNA-binding proteins which bind to telomeric RNAs (TERRA) and regulate their abundance and functions *in vivo*. The findings are published today in the journal *Nature Communications*. The study anticipates the importance of TERRA-associated proteins on telomere biology and telomere diseases, such as cancer and ageing.

Isabel López de Silanes and Martina Stagno d'Alcontres from Maria A. Blasco's research Group at the CNIO found that TERRA are endogenously-bound by a complex array of RNA-binding proteins, which regulate the abundance and location of telomeric RNAs and can have an impact on telomere length and prevention of DNA damage at telomeres.

Telomeres are repetitive DNA sequences that form "capping" structures at the end of mammalian chromosomes protecting them from aberrant rearrangements.

Despite the long-standing belief that telomeres were transcriptionally inactive because of their compact and protective structure, telomeres are transcribed by the DNA-dependent RNA polymerase II giving rise to telomeric transcripts known as TERRA. TERRA are novel structural components of telomeres; they are heterogeneous in size and their abundance is modulated by a number of biological processes including telomeric chromatin status, cellular stresses, as well as during nuclear reprogramming, ontogenesis and cancer. Importantly, TERRA act as potent inhibitors of telomerase activity *in vitro* and are likely to negatively-regulate telomerase activity *in vivo*. However, the molecular mechanisms and factors that control TERRA levels are still largely unknown.

This study carried out by CNIO scientists shows that telomeric RNAs are bound by a complex set of proteins, some of which had been proposed in the past to act as molecular bridges or linkers to recruit telomerase (the enzyme that allows the growth of tumours by maintaining their immortality) to the telomeres. These proteins are now found to affect the levels and cellular localization of TERRA, as well as the ability of telomerase to extend telomeres, and allow proposing a model in which telomeres are subjected to additional levels of regulation, with some of the TERRA-associated proteins having roles in TERRA stability, telomere protection and telomere length regulation.

For the full article, please see:

<http://dx.doi.org/>

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About the CNIO:

The Health Institute Carlos III, an institution belonging to the Spanish Ministry of Science and Innovation, established the Spanish National Cancer Research Centre (CNIO) in 1998. The mission of the CNIO is to carry out research of excellence and to offer innovative technologies within the cancer field to the Spanish National Health System. The CNIO has been directed since its creation by Mariano Barbacid.