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CNIO SCIENTISTS DISCOVER A NEW POTENTIAL ANTI-CANCER TARGET

Madrid, May 17th, 2010 - Scientists of the Spanish National Cancer Research Centre (CNIO) find that the TPP1 telomere-binding protein is essential for telomerase action. Telomerase allows the growth of tumours by maintaining their immortality.

Maria A. Blasco, from the Telomeres & Telomerase Group at the CNIO, has published a study today in the prestigious journal *Developmental Cell* that investigates the role of the telomere-binding protein TPP1 in cell proliferation. Agueda M. Tejera, Martina Stagno d´Alcontres, Paula Martinez, and Rosa Maria Marión, all of them members of the Telomeres & Telomerase Group, also participated in the study.

Some anti-cancer therapies currently tested in clinical trials are focussed on blocking telomerase activity in cancer cells. Telomerase is an enzyme that allows cancer cells to multiply thus making them immortal. Telomerase does this by efficiently binding and elongating the ends of chromosomes, also known as telomeres.

Telomeres are bound by six proteins—TRF1, TRF2, POT1, RAP1, TIN2 and TPP1—which together form a protective complex known as shelterin.

The current investigation demonstrates that TPP1, one of the shelterin components, is the essential element connecting telomerase with telomeres. In the absence of TPP1 telomerase is no longer able to efficiently bind and elongate telomeres.

Under the supervision of Maria A. Blasco and Paula Martínez, Agueda M. Tejera and Martina Stagno d´Alcontres from the Telomeres & Telomerase Group generated a mouse lacking TPP1 protein in epithelial cells. This mouse showed increased telomere damage and shorter telomeres than normal because telomerase was not able to compensate for telomere shortening associated with cell division. As a consequence of this defect, stem cells were not able to regenerate tissues and the mice developed degenerative pathologies. The discovery that TPP1 is essential for the “anti-aging” activity of telomerase was confirmed using nuclear reprogramming experiments.

Nuclear reprogramming consists of generating pluripotent stem cells from differentiated cells, a process that involves telomere elongation by telomerase. This has recently been achieved by the generation of the so-called induced pluripotent stem cells or iPS cells. TPP1-deficient iPS cells were not able to elongate telomeres, a similar phenotype to that of telomerase-deficient iPS cells (Marion et al., *Cell Stem Cell*, 2009).

Maria A. Blasco says that these findings “open new venues for anti-cancer therapies. Until now telomerase was the only telomere-related target in anti-cancer therapies, but this investigation proves that another option would be targeting TPP1”.

For the full article, please see:

http://www.sciencedirect.com/science/journal/15345807

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.