



SCIENCE FOR THE BENEFIT OF HUMANITY

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Human Telomeric Proteins Involved in Cancer and Cellular Aging

RU 671

Technology Summary

Telomeres are repetitive DNA sequences that cap the ends of chromosomes. The primary function of telomeres is to protect chromosome ends from degradation and fusion. Telomeres also appear to play a significant role in cellular aging – each time a cell divides, the mechanism of DNA replication causes the telomeres to gradually shorten until the chromosomes become so frayed that the cell enters a state of irreversible growth arrest, termed senescence. In most cell types, this is normal, however, in certain cell types such as those that make eggs and sperm and also cancer cells, an enzyme called telomerase rebuilds the telomeres after each division to maintain telomere length and prevent the cell from aging. Our scientists have discovered a number of human proteins that interact with the telomeric repeats at chromosomes and studied their role in telomere maintenance and function, which are covered by issued and pending U.S. patent applications. Many of them are also available as tangible materials for research.

1. **RU 671:** The human protein, **Rif1**, which plays an important role in responding to and repairing DNA damage by radiation. Rif1 binds to the ends that are made when DNA is damaged through the direct control of a master regulator of the DNA damage response, the Ataxia Telangiectasia Mutated (ATM) kinase. Their experiments show that Rif1's main role is to prevent cells from replicating their DNA and multiplying further, thus maintaining genomic stability. The radiation-induced binding of Rif1 to DNA breaks is clearly visible as foci by immunofluorescence microscopy. These foci are also indicative of ATM kinase activity, therefore it is foreseeable that a simple and rapid **diagnostic** test of ATM kinase status in tumor samples could be developed. This Rif1 foci formation assay could also be used to **identify compounds that inhibit ATM kinase activity**, which could be used **as radiosensitizers** in radiation oncology. Our scientists are now launching studies to test patients with sporadic and hereditary breast cancer for Rif1 mutations. One population of interest is patients with hereditary breast cancer but no mutations in BRCA1 and BRCA2.

Patent Information

- U.S. Patent 7,507,806

References

- Silverman, *et al.* 2004. *Genes & Dev.*, 18:2108-2119.

Stage of Development

- Discovery; *in vitro* experiments in mammalian and human cells.

Lead Inventor

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