

Lab identifies elusive telomere RNA subunit in single cell model

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The Stowers Institute's Baumann Lab has identified the long-sought telomerase RNA gene in a single-cell research model. Their findings have been posted to the Web site of the journal *Nature Structural & Molecular Biology* and will appear in a future print edition.

Chromosomes shorten with every cell division. In stem cells and in cancer cells, this shortening is compensated by telomerase, an enzyme that adds short repeat sequences to the ends of chromosomes to replenish lost DNA. As telomerase is required for the continued growth of most cancer cells, the enzyme is considered a promising target for new anticancer drugs. A correlation between telomere length and a variety of diseases has further intensified interest in understanding telomerase and its regulation.

The RNA subunit of telomerase is of particular interest as it represents one of the two core components of telomerase and provides the template for the short repeats that are added to the ends of chromosomes. The Baumann Lab is working to understand how telomerase is assembled, how it is recruited to chromosome ends, and how its activity is regulated. These efforts may shed light on the sometimes surprising correlations between telomere shortening and stress, smoking, obesity, and a variety of diseases including cancer and coronary heart disease.

Telomerase RNA has been studied in a variety of simple model organisms, but telomere maintenance turned out to be quite different in these species compared to human cells. Recently, the Baumann Lab used



a biochemical approach to identify and clone the RNA subunit of telomerase in Schizosaccharomyces pombe, or fission yeast.

"The identification of the fission yeast equivalent of the telomerase RNA gene provides us with a critical tool to study telomerase in a genetically tractable, single-cell organism with a telomere maintenance machinery that shares many features with human cells," explained Peter Baumann, Ph.D., Assistant Investigator and senior author on the paper. "We and others had been studying telomerase activity, recruitment, and regulation for several years but the fact that the RNA subunit was unknown in our fission yeast model system severely limited our ability to make progress."

Now that the missing component of the model system has been identified, the Baumann Lab's structural and functional studies are expected to progress rapidly. The lab is now turning its attention to how and where telomerase is assembled from its components in the cell and what processing it must undergo to become active.

Source: Stowers Institute for Medical Research

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