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Jack W. Szostak, PhD – 2009 Nobel Laureate in Physiology or Medicine
Prestigious prize honors Mass. General scientist for role in discovery of telomerase, enzyme that protects chromosome tips

BOSTON – Jack W. Szostak, PhD, of the Massachusetts General Hospital (MGH) Department of Molecular Biology and Harvard Medical School has been named a recipient of the 2009 Nobel Prize in Physiology or Medicine for work predicting and then discovering telomerase, an enzyme that builds and maintains the protective caps at the tips of chromosomes. He shares this year's prestigious scientific award with Elizabeth H. Blackburn, PhD, of the University of California at San Francisco and Carol W. Greider, PhD, of the Johns Hopkins School of Medicine. In 2006 the three researchers shared the Lasker Award for Basic Science for the same work.

The existence of telomeres – molecular caps at the ends of chromosomes – was hypothesized in the 1930s from the observation that broken chromosome fragments fuse with each other, which normal chromosome ends never do. In 1980 Szostak, a yeast geneticist, began a collaboration with Blackburn; they showed that repeated nucleotide sequences she had identified in telomeres of the single-celled protozoan *Tetrahymena* also protected yeast DNA segments from degradation. Their studies led to the discovery that normal yeast chromosomes had a related but distinct structure and that *Tetrahymena* telomeres, when placed in yeast, lengthened by adding new sequences to the end of the DNA. That finding led to the prediction that a new enzyme was adding the protective sequences to the chromosome tips.

Blackburn and Greider went on to isolate telomerase, while Szostak identified a protein essential for maintaining telomeres in yeast, which turned out to be a key component of the enzyme. His work showed for the first time that the inability to add nucleotide repeats to chromosomes led to telomere shortening and eventually cell death. This was the first link between the molecular biology of telomeres and cellular senescence, the aging and death of cells. Although this work was not known

to be relevant to human disease when carried out in the 1980s, subsequent studies of telomeres and telomerase in human cells have shown that the enzyme plays crucial roles in both cancer and aging.

Szostak's research group has followed a different path in recent years, investigating the molecular origins of life. The researchers are seeking to understand how complex chemicals were able to self-assemble and combine to form simple organisms that can reproduce and evolve. Currently they are working to develop simple cell-like structures incorporating both a nucleic acid – such as RNA or DNA – and an enclosing membrane; investigating ways to use the cell's protein-making machinery to create molecules of interest; and using the power of natural selection to create and study new RNA and protein sequences.

Szostak is the Alex Rich Distinguished Investigator in the MGH Department of Molecular Biology, a member of the hospital's Center for Computational and Integrative Biology, a professor of Genetics at Harvard Medical School and a Howard Hughes Medical Institute Investigator. He is a graduate of McGill University and holds a PhD from Cornell University. More information about Szostak and his work can be found at <http://ccib.mgh.harvard.edu/founders-szostak.htm> and <http://genetics.mgh.harvard.edu/szostakweb/>.

Massachusetts General Hospital (www.massgeneral.org), established in 1811, is the original and largest teaching hospital of Harvard Medical School. The MGH conducts the largest hospital-based research program in the United States, with an annual research budget of more than \$550 million and major research centers in AIDS, cardiovascular research, cancer, computational and integrative biology, cutaneous biology, human genetics, medical imaging, neurodegenerative disorders, regenerative medicine, systems biology, transplantation biology and photomedicine.

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