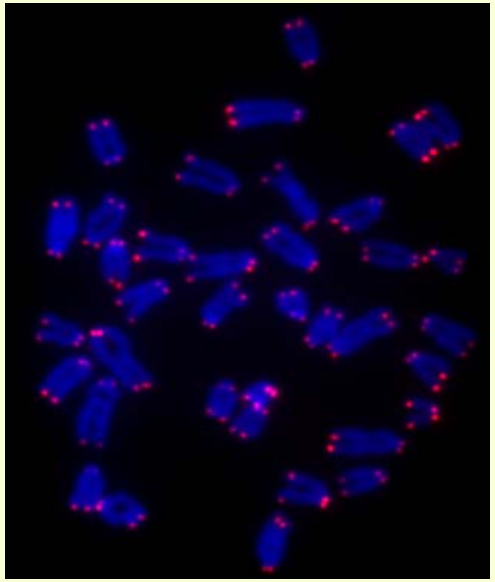
New Publications from Mammalian Genetics Program, Life Sciences Division

Contact: Yie Liu, 865-574-5403 or liuy3@ornl.gov

Funding Source: DOE-OBER (KP14) and ORNL LDRD funds

- Yie Liu, B. Snow, W. Zhou, V. A. Kickhoefer, N. Erdmann, A. Wakeham, M. Gomez, and L. Harrington, “A vault protein, VPARP, is associated with mammalian telomerase and is dispensable in telomerase function and vault structure *in vivo*,” *Molecular and Cellular Biology*, **24**(12), June 2004 (in press).
- N. Erdmann, Y. Liu, and L. Harrington, “Distinct dosage requirements for the maintenance of long and short telomeres in *mTert* mice,” *Proceedings of the National Academy of Sciences*, April 2004 (in press).
- Telomerase, an enzyme, is essential in maintaining the integrity of the end of chromosomes (called "telomere”)
- Dysfunction of telomere could lead to human aging, premature aging syndromes, and cancer
- ORNL identified a novel telomerase component and studied its role in telomerase
- ORNL created a mutant mouse model that produces very low amounts of telomerase; these mice suffer premature aging effects, and so mimic a known human inherited disorder that causes premature aging
- Work confirms a genetic basis for this human disorder in the telomerase gene and supports role of telomerase in human aging and cancer



Fluorescence *in situ* hybridization (FISH) of telomeric DNA (red) localized to ends of mouse chromosomes (blue).

- Two publications have resulted from research on telomerase function in Dr. Yie Liu's laboratory in the Mammalian Genetics Program in ORNL's Life Sciences Division.

New Publications from Mammalian Genetics Program, Life Sciences Division

Two new publications report research on telomerase function in Dr. Yie Liu's laboratory in the Mammalian Genetics Group:

(1) Yie Liu, B. Snow, W. Zhou, V. A. Kickhoefer, N. Erdmann, A. Wakeham, M. Gomez, and L. Harrington, "A vault protein, VPARP, is associated with mammalian telomerase and is dispensable in telomerase function and vault structure *in vivo*," *Molecular and Cellular Biology*, **24**(12), June 2004 (in press).

(2) N. Erdmann, Y. Liu, and L. Harrington, "Distinct dosage requirements for the maintenance of long and short telomeres in *mTert* heterozygous mice," *Proceedings of the National Academy of Sciences*, April 2004 (in press).

Telomerase, an enzyme or protein, is essential in maintaining the integrity of the ends of chromosomes (called "telomeres"); disruption of this function during cell division is implicated in human aging, premature aging syndromes, and cancer. In the *Molecular and Cellular Biology* paper, ORNL and collaborators identified a novel protein to be a key component in the telomerase complex and studied its role in telomerase. In order to study how telomerase works in maintaining telomere, it is critical to know the parts of the telomerase and what they do.

However confirming the role of telomerase disruptions in humans is difficult. In the *PNAS* paper, ORNL and collaborators at the University of Toronto created a mutant mouse that produces very low amounts of telomerase; these mice suffer premature aging effects, and so mimic a known human inherited disorder that causes premature aging. This exciting work confirms a genetic basis for this human disorder in the telomerase gene and supports the role of telomerase in human aging and cancer.

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