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New Telomerase PCR ELISA Offers Simplified, Nonradioactive TRAP Assay for Measuring Telomerase, A Potential Marker for Cancer Research

Boehringer Mannheim is now offering a Telomerase PCR ELISA for the highly sensitive, nonradioactive detection of telomerase activity in extracts from cell cultures and tissue samples.

Telomerase as an important parameter in cancer research

Telomeres, the specialized DNA/protein structures at the end of eukaryotic chromosomes, contain tandemly repeated DNA sequences that are believed to protect genomic DNA from degradation and deleterious recombination events. During normal somatic cell proliferation, telomeric ends are progressively shortened with each replication cycle, which may play a role in limiting the proliferative capacity of normal cells. Germline cells, many tumor cells, and "immortalized" cell lines are believed to circumvent this telomere shortening using telomerase, a ribonucleoprotein that adds new repeats to the ends of chromosomes. Telomerase activity has recently been identified in many cancers (e.g., prostate cancers [1], advanced-stage breast cancers [2], neuroblastomas [3], and primary lung cancer tissues [4]) that have been confirmed by other methods (*e.g.*, histochemical staining). Thus, telomerase reactivation may allow cells to escape from the proliferative limitations of cellular senescence and could be further investigated as a potential marker for the development of malignant tumor cells.

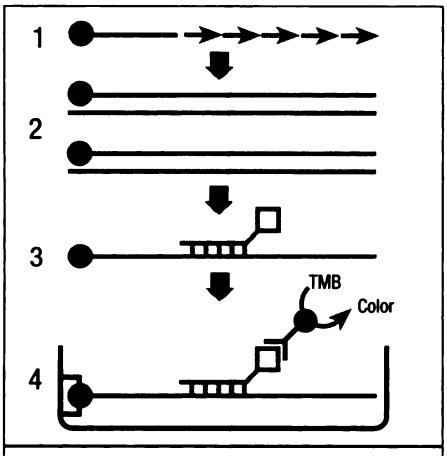

Figure 1. Detection of telomerase activity with the Telomerase PCR ELISA.

Step 1. Telomerase, if present, adds multiple 6-nucleotide telomeric repeats to a biotinylated synthetic primer.

Step 2. The telomerase reaction product is amplified by PCR, using a biotinylated primer.

Step 3. After denaturation, the PCR product hybridizes to a digoxigenin-labeled probe specific for the telomeric repeat.

Step 4. The DNA hybrid binds to a streptavidin-coated microtiter plate, and anti-digoxigenin-peroxidase and TMB substrate generate a colored product measurable with a microplate reader.

Note: If desired, the TRAP reaction product from Step 2 can also be detected by the traditional gel electrophoresis method.

Telomerase PCR ELISA improves upon previous TRAP assays

Telomerase activity is most frequently detected by the Telomeric Repeat Amplification Protocol (TRAP) of Kim *et al.* (5), in which the telomerase-reaction product is amplified by PCR. However, the conventional TRAP assay achieves full sensitivity only when performed with a hazardous radioactive label, and visualization of results requires time-consuming gel electrophoresis and autoradiography. The new Telomerase PCR ELISA*,† combines a one-step/one-tube TRAP assay with nonradioactive detection in a highly sensitive photometric ELISA (Figure 1).

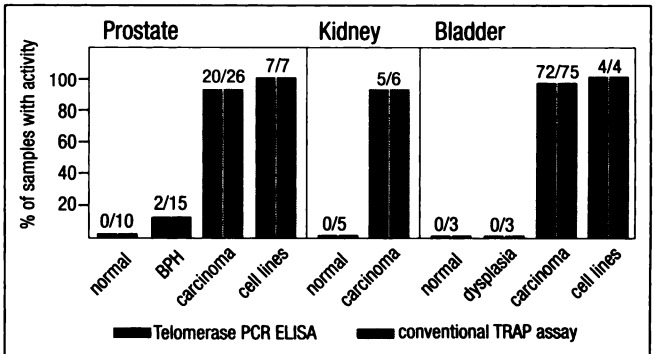

Figure 2. Correlation of results obtained with the Telomerase PCR ELISA and conventional, radioisotopic TRAP assays. Samples from known carcinomas, normal specimens (negative control), benign prostatic hyperplasia (BPH) specimens, and immortalized cell lines were tested in parallel with the Telomerase PCR ELISA and conventional, radioisotopic TRAP assays. In all sample types, the two methods were able to identify the same number of samples featuring telomerase activity.

Data provided by M. Müller and R. Heicappell (6) and by H. J. Sommerfeld.

Easy-to-use ELISA delivers results in less time

The Telomerase PCR ELISA delivers results within 6 hours, eliminating the need for laborious, time-consuming gel electrophoresis and autoradiography techniques. Its ready-to-use TRAP reaction mix (telomerase substrate, amplification primers, nucleotides, *Taq* DNA polymerase, reaction buffer) eliminates the need to prepare multiple solutions and minimizes the risk of assay failure caused by contamination. Up to 96 TRAP reactions can be simultaneously analyzed with an ELISA plate reader.

Sensitive results correspond closely with those of radioactive TRAP assays

Besides avoiding the use of hazardous radioisotopes, the Telomerase PCR ELISA produces sensitive results comparable to those of the radioisotopic TRAP assay (Figure 2). The kit's optimized detection probe and hybridization conditions maximize both specificity and sensitivity. Additionally, optimized primer sequences eliminate the need for "hot start" PCR while avoiding amplification artifacts (*e.g.*, primer dimers).

The Telomerase PCR ELISA is currently available

The Telomerase PCR ELISA (96 tests; Cat. No. 1 854 666) is now available from Boehringer Mannheim Biochemicals representatives. Additional information can also be found at http://biochem.boehringer-mannheim.com.

References:

1. Sommerfield, H.J. *et al.* (1996) *Cancer Research* **56**:218-222.
2. Hiyama, E. *et al.* (1996) *J. National Cancer Institute* **88**:116-122.
3. Hiyama, E. *et al.* (1995) *Nature Medicine* **1**:249-255.
4. Hiyama, K. *et al.* (1995) *J. National Cancer Institute* **87**:895-902.
5. Kim, N. W. *et al.* (1994) *Science* **266**:2011-2015.
6. Müller, M. *et al.* (1996) *Int. J. Oncology* **9**: *in press.*

†Licensed from Geron Corporation. Patents pending.

*Purchase of this product is accompanied by a limited license to use it in the Polymerase Chain Reaction (PCR) process in conjunction with a thermal cycler whose use in the automated performance of the PCR process is covered by the up-front license fee, either by payment to Perkin-Elmer or as purchased, i.e., an authorized thermal cycler.

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Emory University Cancer Epidemiologist

The Georgia Center for Cancer Statistics in the Department of Epidemiology, Rollins School of Public Health of Emory University, is seeking a research track Assistant, Associate, or Full Professor, depending upon qualifications, to join our group of cancer epidemiologists as Director of the Georgia Cancer Registry. Primary responsibilities include the continued development and operation of the Georgia Cancer Registry.

Requirements for the position include: 1) a Doctoral degree in epidemiology, biostatistics, or related field and 2) experience in the operation and supervision of a central cancer registry. Teaching experience and a publication record are also desirable.

Interested applicants should submit a letter of interest, a curriculum vitae, and a list of at least 3 references to: Jonathan M. Liff, Ph.D., Department of Epidemiology, Rollins School of Public Health of Emory University, 1518 Clifton Road, Room 420, Atlanta, Georgia 30322.

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Cancer Registry Manager/Georgia Center for Cancer Statistics

The Georgia Center for Cancer Statistics, located at Emory University, is seeking a General Manager for our cancer registry program. We operate the Georgia Cancer Registry, the Metropolitan Atlanta and Rural Georgia SEER program, and the Savannah River Region Health Information System (Georgia component). Primary responsibilities include management and supervision of the cancer registry operations.

Requirements include experience in the operation or supervision of a central cancer registry. Master's degree preferred for a faculty level position in the Rollins School of Public Health at Emory University.

Interested applicants should submit a letter of interest, a curriculum vitae, and a list of at least 3 references to: Jonathan M. Liff, Ph.D., Department of Epidemiology, Rollins School of Public Health of Emory University, 1518 Clifton Road, Room 420, Atlanta, Georgia 30322.

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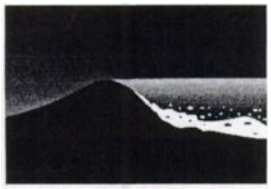

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Applicants are encouraged to submit abstracts for presentation.

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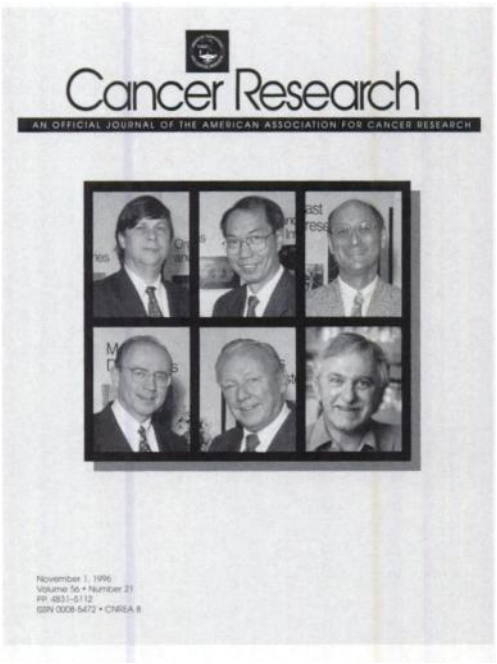

The General Motors Cancer Research Foundation has named six researchers as recipients of its three annual awards, according to an announcement by Joseph G. Fortner, President of the Foundation. Each award is being shared by two recipients this year.

The Charles F. Kettering Prize for outstanding contributions to the treatment of cancer was awarded to Patrick C. Walsh (*bottom left*), Director of the Department of Urology, Johns Hopkins University, and Malcolm A. Bagshaw (*bottom center*), Professor Emeritus of Cancer Biology at Stanford University. They were instrumental in developing modern prostate cancer treatment. Dr. Walsh developed ways of removing prostate tumors that greatly reduced the risk of impotency and incontinence, and he has done much to characterize familial and genetic factors responsible for this neoplasm. Dr. Bagshaw showed that high-dose, small-field radiation could allow selected patients to undergo potentially curative therapy without the need for surgery. Prior to his work, prostate cancer was considered by many to be radio-resistant. Dr. Bagshaw is an emeritus member of the American Association for Cancer Research (AACR).

Winners of the Charles S. Mott Prize for outstanding contributions to research on the causation and prevention of cancer were Paul L. Modrich (*bottom right*), Professor of Biochemistry and Investigator at the Howard Hughes Medical Institute, Duke University Medical Center, and Richard D. Kolodner (*top right*), Professor of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, and Chief of Human Cancer Genetics at the Dana-Farber Cancer Institute. They are unraveling the mechanism of DNA "mismatch repair" and its relationship to hereditary nonpolyposis colon carcinoma (HNPCC), a common cancer susceptibility syndrome possibly affecting as many as one out of every 200 people in the United States. For the past 14 years, they have made enormous strides in providing markers for HNPCC and in identifying enzymes to restore "mismatch repair." According to Dr. Fortner, the lack of these repair enzymes is a potential marker for risk of other cancers and could aid in diagnosis and treatment. Dr. Kolodner is an active member of the AACR, and he has been serving on the *Cancer Research* Editorial Board since 1995.

The Alfred P. Sloan, Jr. Prize for pioneering efforts in basic science contributing to cancer research was shared by Mark M. Davis (*top left*), Investigator at the Howard Hughes Medical Institute and Professor of Microbiology and Immunology at Stanford University School of Medicine, and Tak W. Mak (*top center*), Senior Scientist of the Division of Cellular and Molecular Biology at the Ontario Cancer Institute. The Sloan Award winners are helping to bring medicine closer to the ultimate goal of developing vaccines to combat cancer. Their work delineated how T-cells recognize foreign or abnormal cells and identified the genes coding for the antigen receptors on T-cells. They not only clarified the role of the T-cell receptor in immune reactions to pathogens and tumor cells, but they also demonstrated that these genes are involved in chromosomal translocations in T-cell malignancies, facilitating the cloning of numerous new oncogenes and antioncogenes by many investigators. Dr. Mak is an active member of the AACR. He has served on the Program Committee (1992), and he chaired an AACR Special Conference, "The Molecular Basis of Tumor Immunology," in May 1990. Moreover, he served as an Associate Editor for Cancer Research for nearly a decade (1986–95).

Each of the General Motors Cancer Research Foundation awards includes $100,000 and a commemorative gold medal. The Foundation was established in 1978. In addition to sponsoring its three annual awards, the Foundation holds a scientific conference each year on the latest research findings on the causes and treatment of cancer. The 1996 conference, "Origins of Breast and Prostate Cancer," focused on the role of genetics, hormones, and environment in breast and prostate cancer.

We are indebted to the Foundation, the recipients of the awards, and Ayer Public Relations for the photographs and information used for this cover feature.

Sidney Weinhouse