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.

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/tube TRAP assay with nonradioactive detection in a highly sensitive photometric ELISA (Figure 1).

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:

^ 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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Disrupted Transcription Factors in Cancer

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SCIENTIFIC PROGRAM

Keynote Address
Carlo M. Croce / Philadelphia, PA

Basic Transcriptional Mechanisms
Robert Tjian / Berkeley, CA
Danny F. Reinberg / Piscataway, NJ
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Development, Negative Regulators
Luc St-Onge / Gottingen, Germany
David M. Livingston / Boston, MA
Eric N. Olson / Dallas, TX
Stuart Orkin / Boston, MA
Jean Y. J. Wang / La Jolla, CA
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Christopher T. Denny / Los Angeles, CA
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Cory Abate-Shen / Piscataway, NJ

Leukemias I
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A. Thomas Look / Memphis, TN
Richard J. Baer / Dallas, TX
Gary Gilliland / Boston, MA
Mark P. Kamps / La Jolla, CA

Solid Tumors II
Riccardo Dalla Favera / New York, NY
Frederic G. Barr / Philadelphia, PA
Garrett M. Brodeur / Philadelphia, PA
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Leukemias II
Janet D. Rowley / Chicago, IL
Ronald M. Evans / La Jolla, CA
Paul P. Liu / Ann Arbor, MI
Yoshiaki Ito / Kyoto, Japan
Laurie H. Glimcher / Boston, MA
Ivan Horak / Berlin, Germany

Clinical Applications
Samuel Waxman / New York, NY
Pier Pellicci / Milan, Italy
H. Phillip Koeffler / Los Angeles, CA

Applicants are encouraged to submit abstracts for poster presentation.

Information and Application Forms
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Basic and Clinical Aspects of Lymphoma

January 10-14, 1997
Renaissance Esmeralda Resort
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The New Entities and Classification
Nancy L. Harris / Boston, MA
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Richard I. Fisher / Maywood, IL

Lymphomagenesis and Etiology
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Lymphoma Associated with Immunodeficiency
Daniel Knowles / New York, NY
Lode J. Swinnen / Maywood, IL
Alexandra M. Levine / Los Angeles, CA

Genetic Abnormalities in Lymphoma
Raju S. K. Chaganti / New York, NY
Riccardo Dalla-Favera / New York, NY
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Cell Adhesion and Cell Signaling/
Molecular and Homing Receptors
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Clinical trials of cancer therapeutic and preventive agents are complicated and costly. Poor design of some aspect of a trial can make it impossible to reach a definitive conclusion about the effectiveness of a promising new agent and can lead to the abandonment of potentially useful lines of research. On the other hand, many well designed clinical trials are in progress every day, and their results are presented at meetings and in the pages of the American Journal of Clinical Oncology for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO). Furthermore, training the next generation of clinical cancer researchers is a high priority of both societies. AACR and ASCO have therefore combined their substantial intellectual and administrative resources to organize a one-week summer workshop that introduces clinical fellows and junior faculty to the principles of clinical trials design. This training is intended to raise the standard of clinical trials performed and thus to facilitate the translation of advances in the laboratory to the bedside.

This jointly sponsored workshop, entitled “Methods in Clinical Cancer Research,” took place from August 17-22, 1996, in Park City, Utah. The idea originated in the Special Conferences Committee of the AACR, and its development was encouraged by the National Cancer Institute’s Cancer Training Branch which has oversight of the AACR’s two other summer training workshops: “Molecular Biology in Clinical Oncology” and “Histopathobiology of Neoplasia.” During the Summer of 1995 the officers of AACR and ASCO met to identify potential new areas of collaboration between the two societies, and this workshop was considered to be a logical choice for the first joint effort.

To organize the workshop both AACR and ASCO appointed a chairperson and four members to a joint Program Committee. Representing the AACR were Daniel D. Von Hoff, Chairperson, Cancer Therapy and Research Center (CTR), San Antonio, TX; David S. Alberts, University of Arizona Cancer Center, Tucson, AZ; Gary M. Clark, CTRC; Merrill J. Egorin, University of Maryland Cancer Center, Baltimore, MD; and Sandra J. Horning, Stanford University School of Medicine, Palo Alto, CA. ASCO’s appointments to the Program Committee were Charles A. Coltman, Jr., Chairperson, CTRC; Janice P. Dutcher, Albert Einstein Cancer Center, New York, NY; Michael A. Friedman, U.S. Food and Drug Administration, Rockville, MD; Steven Pantazis, Johns Hopkins University School of Medicine, Baltimore, MD; and Mark J. Ratain, University of Chicago, Chicago, IL. (Martin N. Raber, UT-M.D. Anderson Cancer Center, Houston, TX, was the initial ASCO Program Committee Chairperson but had to withdraw from this position because of personal circumstances. Dr. Raber had made substantial contributions to the development of the program in the Summer and Fall of 1995.)

In a series of meetings the Program Committee refined the purposes of this workshop, determined the most appropriate audience, and then developed a suitable format and daily schedule. It was felt that the best use of the resources being applied to the workshop would be to limit the student body to clinical researchers in the relatively early stages of their careers. Intensive training at this stage would help these scientists to avoid errors that more experienced researchers could readily avoid. The audience selected therefore was oncology fellows and clinical researchers at the level of instructor or assistant professor who had completed their fellowships no more than five years earlier. For the first workshop, there were 67 oncology fellows and 37 clinical researchers at the junior faculty level chosen to participate.

To achieve the basic purpose of providing an intensive week of training in clinical trials design the basic daily schedule included three to four hours of lectures by leaders in the various scientific areas relevant to clinical cancer research plus two hours of “small group discussion sessions” in which 20–25 students met with a panel of faculty members to examine important topics such as biostatistics and pharmacology in detail and to work through case studies highlighting problems in these areas.

To ensure that this workshop has a significant impact beyond the week it actually takes place, the organizers added a third vital component to the program: a requirement that each student draft and submit an actual clinical trial protocol while in attendance. During the application process, candidates described the protocols they intended to submit, and their mentors were required to sign statements that they would allow students to conduct the trials when they returned from the course. The organizers carefully scrutinized these sections of the application packages when they selected the students who were actually invited to attend. In Park City, students devoted considerable time to the preparation of these protocols. They met in groups of 4–8 with individual faculty members on four occasions during the week to review their progress, thus further encouraging student-faculty interaction.

Ongoing evaluation of this program is extremely important. Organizers will adjust the workshop content each year in response to questionnaires completed by students and the results of a test administered at both the beginning and the end of the workshop. Long-term evaluation will be facilitated by follow-up of the progress of the students in the implementation of their protocols. The faculty has established a series of checkpoints (including IRB approval, funding, completion, presentation of data, and publication of data) against which students will be measured.

This program is intended to be held each year, and funding has already been secured for 1997 and 1998. In 1996, it benefited from the great generosity of four sponsors: The National Cancer Institute, Amgen, Inc., Bristol-Myers Squibb Oncology, and Hoechst Marion Roussel. AACR and ASCO are grateful to all the faculty and committee members, particularly the large number of students who made the course successful not just by making excellent presentations, but by spending many hours of time with students writing their protocols. This interaction is ongoing. Finally, we acknowledge in particular Drs. Von Hoff and Coltman whose broad knowledge of this important area of cancer research is matched only by their passion for improving the quality of clinical trials design and, of course, by their commitment to conquering cancer.