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 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.

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.

Helping biomedical research become medical practice.

BOEHRINGER MANHEIM
AACR SPECIAL CONFERENCE IN CANCER RESEARCH

Basic and Clinical Aspects of Breast Cancer

March 7-12, 1997
The Keystone Resort, Keystone, Colorado

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Karen S. H. Antman / New York, NY
Mary-Claire King / Seattle, WA

SCIENTIFIC PROGRAM

Keynote Addresses
Mary-Claire King / Seattle, WA
Karen S. H. Antman / New York, NY

Basic Biology of the Breast
José Russo / Philadelphia, PA
Marc E. Lippman / Washington, D.C.
C. Kent Osborne / San Antonio, TX
Charles W. Daniel / Santa Cruz, CA

Molecular and Cellular Aspects of Breast Cancer
Jerry W. Shay / Dallas, TX
Mina J. Bissell / Berkeley, CA
Martha R. Stampfer / Berkeley, CA
Joyce M. Slingerland / Toronto, Ontario, Canada

Genetic Predisposition to Breast Cancer
David E. Goldgar / Lyon, France
P. Andrew Futreal / Durham, NC

Mechanisms of Hormone Action
V. Craig Jordan / Chicago, IL
Myles A. Brown / Boston, MA
Kenneth S. Korach / Research Triangle Park, NC

BRCA1 and BRCA2 Function/Biochemistry
Roy A. Jensen / Nashville, TN
Wen-Hwa Lee / San Antonio, TX
David M. Livingston / Boston, MA
Frank J. Califone / Thousand Oaks, CA

Experimental Models of Breast Cancer
Tak W. Mak / Toronto, Ontario, Canada
Roger W. Wiseman / Research Triangle Park, NC
Michael N. Gould / Madison, WI

Epidemiology of Breast Cancer
Walter C. Willett / Boston, MA
Maureen Henderson / Seattle, WA
Malcolm C. Pike / Los Angeles, CA
Mary S. Wolff / New York, NY

Clinical Aspects of Breast Cancer
Judy E. Garber / Boston, MA
Jeffrey T. Holt / Nashville, TN
M. John Kennedy / Baltimore, MD

Applicants are encouraged to submit abstracts for poster presentation.

Application deadline: January 20, 1997

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MARCH 7-12, 1997
Basic and Clinical Aspects of Breast Cancer
Chairpersons: J. Carl Barrett, Research Triangle Park, NC; Karen S.H. Antman, New York, NY; Mary-Claire King, Seattle, WA
Keystone Resort, Keystone, CO

APRIL 12-16, 1997
88th Annual Meeting
Chairperson: Frederick P. Li, Boston, MA
Co-Chairpersons: Clara Derber Bloomfield, Buffalo, NY; Stephen H. Friend, Seattle, WA
San Diego Convention Center, San Diego, CA

JUNE 7-11, 1997
Cancer of the Central Nervous System
Conference with Neurosurgery Joint Section on Tumors
Chairpersons: Peter McL. Black, Boston, MA; Webster K. Cavenee, La Jolla, CA
Loew's Coronado Bay Resort, San Diego, CA

SEPTEMBER 9-13, 1997
Molecular Genetics of Cancer
Conference with the European Association for Cancer Research
Chairpersons: Eric J. Stanbridge, Irvine, CA; Walter Bodmer, Oxford, England
Hertford College, Oxford, England

SEPTEMBER 26-30, 1997
Tumor Suppressor Genes
Chairpersons: Stephen H. Friend, Seattle, WA; Philip Branton, Montreal, Quebec, Canada
Victoria Conference Centre, Victoria, BC, Canada

OCTOBER 17-21, 1997
Gene Regulation in Differentiation and Development
Chairpersons: Robert Eisenman, Seattle, WA; Elaine V. Fuchs, Chicago, IL
The Sagamore Resort, Bolton Landing (Lake George), NY

DECEMBER 1997
Epigenetics of Cancer
Chairperson: Peter A. Jones, Los Angeles, CA
Location in Puerto Rico to be Announced

JANUARY 9-13, 1998
Colorectal Cancer — Biology, Treatment, and Prevention
Joint Meeting with the American Society of Clinical Oncology
Chairpersons: Robert J. Mayer, Boston, MA; One Additional Chairperson to be Announced
Renaissance Esmeralda Resort, Indian Wells (Palm Springs), CA

JANUARY 1998
Angiogenesis and Cancer
Chairpersons: Judah Folkman, Boston, MA; Michael Klagsbrun, Boston, MA
Location in Orlando, FL to be Announced

FEBRUARY 16-21, 1998
Innovative Molecular Biology Approaches to the Prevention, Diagnosis, and Therapy of Cancer
Joint Meeting with the Japanese Cancer Association
Chairpersons: Edward Bresnick, Worcester, MA; Kaoru Abe, Tokyo, Japan
Maui Marriott Resort, Maui, HI

AACR members will receive brochures on the above conferences as soon as they are available. Nonmembers should call or write:
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By the time Dr. Berd’s group moved to Thomas Jefferson University in 1984, it was clear that a new approach was necessary. With Dr. Maguire’s encouragement, Dr. Berd rediscovered the phenomenon of autoimmunity induced by immunization with cells modified by a hapten. Several investigators, especially Gene M. Shearer at the NIH, had shown that treatment of murine cells with trinitrophenyl (TNP) rendered them highly immunogenic in syngeneic hosts. Remarkably, immunization with TNP-modified cells sometimes resulted in the generation of T lymphocytes that recognized unmodified syngeneic cells as well. This phenomenon was recently elucidated on the level of cell-bound peptides by Hans Ulrich Weltzien’s group in Freiburg, Germany (Eur. J. Immunol., 25: 2788, 1995).

In September 1988, Dr. Berd’s group was the first to treat a patient with a vaccine consisting of irradiated autologous melanoma modified with the hapten dinitrophenyl (DNP). Dr. Berd retained elements of his previous program, specifically the use of BCG as an immunological adjuvant and pretreatment with low dose cyclophosphamide. The result was unexpected and, to their unprepared minds, quite wondrous. Over a period of 4 months, the multiple skin metastases in this patient developed an inflammatory response: the tumors became erythematous, warm, and tender, and eventually ulcerated with drainage of necrotic material. Biopsy of these inflamed tumors showed infiltration of lymphocytes with focal tumor cell necrosis (Cancer Res., 51: 2731, 1991).

It soon became apparent that this initial patient was not an anomaly, as the development of tumor inflammatory responses was observed in about half of the patients with superficial metastases. The photomicrograph on the cover, taken by George F. Murphy, then of the University of Pennsylvania School of Medicine, illustrates a typical histology of lymphocytes exhibiting satellitosis around a central degenerating melanoma cell (Cancer Immunol. Immunother., 39: 141, 1994). Subsequently, Dr. Berd determined that the lymphocytes were T cells, predominantly CD8+, that expressed cell surface markers indicative of activation. A very productive collaboration with Giorgio Parmiani and Marialuisa Sensi in Milan has demonstrated that these T cells have been clonally expanded (J. Clin. Invest., in press, 1997) as a result of stimulation by an as yet uncharacterized tumor antigen.

Despite these tumor inflammatory responses, autologous DNP-vaccine only rarely causes clinically defined regression of metastases. Recent work, in collaboration with Edmund C. Latimore and Takami Sato, suggests that production of the anti-inflammatory cytokine IL-10 by melanoma cells might be responsible by suppressing the proliferation of T cells in the tumor site (Clin. Cancer Res., 2: 1383, 1996). On the other hand, autologous DNP-vaccine has produced promising clinical results in melanoma patients with micrometastatic disease (Ann. NY Acad. Sci., 69: 147, 1993). Although these trials are still in progress, 5-year survivals of about 60% in patients with stage 3 melanoma with large, resectable regional lymph node metastases are being seen. This compares to an expected survival of 20–25% with surgery alone (J. Clin. Oncol., 14: 7, 1996). A multi-institutional, randomized trial of the DNP-vaccine as postsurgical adjuvant therapy will be initiated this year, sponsored by AVAX Technologies, a biotechnology company based in Kansas City, MO.

Dr. Berd has published over 57 original research articles and 26 reviews. He has served on many government advisory groups and belongs to several professional societies, including the American Association for Cancer Research (AACR), of which he has been an active member since 1977.

Sidney Weinhouse

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