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ODAC Recommends TICE BCG Approval For Recurrent Bladder Cancer Prevention

Advisors to FDA recommended marketing approval for a BCG vaccine for prevention of bladder cancer and letrozole for treatment of advanced breast cancer.

The FDA Oncologic Drugs Advisory Committee voted 9-1, with one abstention, to recommend marketing approval for TICE BCG, sponsored by Organon Teknika Corp., for intravesical installation for prophylaxis against recurrent papillary carcinoma of the bladder.

(Continued to page 2)

In Brief

Parkinson To Leave CTEP For Novartis; FTC To Permit Sandoz, Ciba-Geigy Merger

DAVID PARKINSON was named vice president, oncology therapeutics, at **Novartis AG.**, a company being formed through a merger of Ciba-Geigy Ltd. and Sandoz Inc. Parkinson, acting director of the NCI Cancer Therapy Evaluation Program, said he plans to leave the Institute later this month. At the newly formed Novartis, Parkinson will head oncology drug development in North America. "I am interested in developing treatments for cancer, and at Novartis, the opportunities for doing this are unparalleled," Parkinson said to **The Cancer Letter**. Parkinson, who joined NCI six years ago, will be based in East Hanover, NJ. . . . **GREGORY BURKE,** former FDA official who headed US oncology drug development at Sandoz, is moving to Basel, where he will head worldwide development of oncology drugs for the newly formed Novartis. . . **THE FEDERAL TRADE COMMISSION** earlier this month announced that it would permit the $63 billion merger between Ciba and Sandoz, provided that the companies carry out several divestitures and license to other entities several patents for gene therapy technologies. The deal involves **Chiron Corp.**, which is partly owned by Ciba. . . . **CLINICAL RESEARCH SEED GRANTS** are available, sponsored by the Cancer Research Institute, of New York City, to support phase I or phase I/II trials testing novel immunotherapies for the treatment of advanced prostate cancer. Grants will be in the amount of $150,000 over two years. Deadline for applications, including clinical protocol, is April 15. Contact Lynne Harmer, Director of Grants Administration, Cancer Research Institute, 681 Fifth Ave., New York, NY 10022-4209, tel: 212-688-7515, fax: 212-832-9376, email: cancerres@aol.com.

FDA Advisors OK Marketing For TICE BCG And Femara

(Continued from page 1)

In a second action, the committee voted 10-0, with one abstention, to recommend marketing approval for Femara tablets (letrozole), sponsored by Ciba-Geigy, for the treatment of advanced breast cancer in women with natural or artificially induced postmenopausal status, following antiestrogen therapy.

In another development at the Dec. 16 meeting, cancer patient representatives became voting members of the committee for the first time. The patient representatives for the meeting were James Schultz, of the American Foundation for Urological Diseases, Prostate Cancer Support Group, and Sandra Zook-Fischler, of Self-Help for Women with Breast Cancer.

SWOG Results Key To BCG Recommendation

TICE BCG, an attenuated, live culture preparation of the Bacillus of Calamette and Guerin strain of Mycobacterium bovis, was approved by FDA in 1990 for carcinoma in situ of the bladder. However, TICE BCG is widely used in the US off-label for prevention of bladder tumor recurrence.

To obtain FDA marketing approval for this indication, Organon Teknika submitted data from two prospective, randomized, controlled studies to the agency. The trials were the Nijemegen study, conducted in the Netherlands, and a trial conducted in the US by the Southwest Oncology Group. Both studies compared TICE BCG with Mutamycin (mitomycin C, MMC), by Bristol-Myers Squibb Co. Both enrolled patients with transitional cell carcinomas, the most common type of bladder tumor.

The SWOG trial (SWOG 8795) enrolled 469 patients, of which 447 were eligible. The recurrence rate for patients taking TICE BCG was 40.3 percent, compared to 54.3 percent for those taking MMC ($p=0.017$).

Median time to recurrence was 44 months for the BCG group, compared to 22 months for the MMC group. Of the BCG group, 7.8 percent progressed while on therapy, compared to 12.9 percent of those taking MMC.

Nearly half the patients enrolled in the SWOG trial had TaG1 tumors, said Donald Lamm, of SWOG. Of those patients, 52 percent recurred while taking BCG, while 60 percent recurred while taking MMC. The times to recurrence were 36 months for those on BCG and 13 months for those on MMC. The differences were not statistically significant, but indicated a trend favoring BCG, Lamm said.

Of those patients with CIS, 55 percent responded to BCG, while 46 percent responded to MMC.

TICE BCG resulted in more side effects than MMC, including dysuria, fever, malaise, and cystitis. About 5 percent of patients taking BCG will develop serious toxicity, Lamm said.

Organon recommends TICE BCG for selected patient groups: those with grade 3 TCC, Ta or T1; stage T1 TCC, grades 1 through 3; recurrent disease, grade 2; or multiple Ta, grade 1 tumors, with recurrence despite resection.

An analysis of the SWOG trial by FDA agreed with the company's presentation that TICE BCG was superior to MMC in reducing the tumor recurrence rate and median disease-free survival.

However, FDA concluded that TICE BCG was not equivalent, but inferior to MMC in the Nijemegen study, agency reviewers Sheldon Morris and Richard Steffen said. In addition, FDA was concerned about the use of MMC as a comparison, because the drug has not been approved for this indication.

In the Nijemegen trial, with 469 patients, only 22 percent had TaG1 tumors. The trial compared three treatment arms: TICE BCG, BCG-RIVM, and

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MMC. Tumor recurrence rate was 44 percent for patients on TICE BCG, 34 percent for BCG-RIVM, and 29 percent for MMC. Median disease-free survival was 2.8 years for those on TICE BCG, and was not reached for the other two arms.

For patients with high grade tumors, those treated with TICE BCG had a 47 percent recurrence rate, compared to 36 percent for BCG-RIVM and 30 percent for MMC. The difference was statistically significant (p=0.04).

Michael Hanna, of Organon Teknika, noted that there were several differences between the studies, neither of which were sponsored by Organon. The Nijemegen study did not select patients, was not stratified, and had no provision for maintenance therapy of BCG.

The SWOG study selected for high risk patients, based on the grade, stage, and rate of tumor recurrence. The SWOG trial also was stratified according to those patients with CIS and those without, and included nine months of maintenance therapy of BCG. In addition, the dose of mitomycin C used by the two groups ranged from 0.6 mg/ml in Nijemegen to 1 mg/ml in SWOG, Hanna said.

ODAC members said that, although the Nijemegen trial did not prove TICE BCG activity in the prevention and recurrence of Ta and T1 tumors, the SWOG study did prove the drug's activity, and overall, the data supported the safety and efficacy of the drug. Many committee members said the indication should not be restricted, though they personally would not recommend using TICE BCG to prevent grade 1 tumors.

FDA asked the committee for recommendations about methods to minimize the risk of nosocomial infection. The committee said labeling could include a warning about not mixing BCG under the same hood as chemotherapeutic agents. The company said the risk of infection is minimized by a new needle-free administration device for TICE BCG.

Femara Trials Support Higher Dose

Ciba-Geigy sponsored three pivotal trials of Femara, an aromatase inhibitor, involving 550 to 600 patients in each study. The company submitted final results of the study AR/BC2 and early results from the study AR/BC3 to FDA. Results for the third study, PO2, are not expected until December 1997.

Patients in all three studies were randomized to one of three treatment arms: 2.5 mg Femara, 0.5 mg Femara, or comparable doses of either Megace (megestrol, Bristol-Myers Squibb) or Cytadren (aminoglutethimide, Ciba-Geigy). The trials included postmenopausal women with advanced breast cancer with objective disease progression or relapse on antiestrogens, measurable or evaluable disease, or positive, estrogen or progesterone receptors.

The primary endpoint of the trials was objective response rate, verified by an independent, blinded external peer review group using UICC criteria. In the AR/BC2 trial, objective response rates were 34 percent for 2.5 mg Femara, compared to 13 percent for 0.5 mg Femara and 16 percent for Megace or Cytadren. In the AR/BC3 study, objective response rates were 18 percent for 2.5 mg Femara, 17 percent for 0.5 mg Femara, and 11 percent for the other two hormonal therapies.

In both trials, the higher dose of Femara had a duration of response 2 to 2.5 times longer than the other agents. The higher dose also had a longer time to progression and time to treatment failure. These results were statistically significant. Survival results and quality of life did not show a statistically significant benefit for 2.5 mg of Femara, but the trend was in favor of the higher dose.

In the two studies, Femara had significantly fewer serious adverse events, as well as discontinuations of therapy, cardiovascular events, and weight gain over 5 percent. Patients on Femara did have an increased incidence of mild to moderate nausea.

FDA reviewer Genevieve Schecter presented data showing that the 2.5 mg dose of Femara was superior to other hormonal therapies in objective response, duration of response, median survival, and days to progression. The FDA analysis also found that Femara had a better safety profile for serious adverse events than other hormonal therapies.

The major issue raised by FDA was whether an antiestrogen withdrawal effect could skew results in favor of Femara. Patients were allowed to enroll the day after ending antiestrogen therapy. Patients who had a partial response to antiestrogen therapy or who had stopped using it less than 60 days before enrolling in the Femara trials were at risk of experiencing an antiestrogen withdrawal effect, Schecter said.

Schecter noted that more than 30 percent of the patients enrolled in the studies were over age 70,

and an additional 50 percent were between the ages of 56 and 70. The remaining 20 percent were between 25 and 55. More than 60 percent of the patients had one site of disease, while 40 percent had multisite tumors. About 60 to 70 percent of the patients had not had chemotherapy, while about 32 percent had undergone adjuvant therapy, 53 percent had other treatment, and 8 to 14 percent had undergone both therapies. Most patients had been in remission for two years or more when the cancer recurred.

ODAC members praised the design of the studies and commended the company for including a large number of elderly patients in the trials.

The committee voted unanimously that tamoxifen withdrawal should not have an impact on the study results. The committee voted 6-5 that future studies should require a one month interval between antiestrogen discontinuation and the beginning of a clinical trial. Committee members who voted against this requirement said they were afraid it would cause some women not to participate in clinical trials.

US Appeals Court Dismisses Bernard Fisher's Privacy Suit

A three-judge panel of the US Court of Appeals dismissed the suit in which cancer researcher Bernard Fisher claimed that NCI and NIH had violated his rights under the Privacy Act by flagging his publications in government-run databases.

The flags, placed in the databases during the controversy surrounding the National Surgical Breast and Bowel Project, contained the words "scientific misconduct." Fisher was never found to have committed any wrongdoing.

In a ruling Nov. 27, the panel of the US Court of Appeals for the District of Columbia said "the merits of the parties' positions [were] so clear as to warrant summary action."

The fundamental issue in Fisher's case has been the definition of a "system of records" in the Privacy Act of 1974, a law that requires the government to maintain accurate information about individuals and limits disclosures of such information.

While Fisher's suit claimed that the flags in the databases referred to him personally, the government maintained that the flags referred to the data in the articles, and for this reason not covered by the Privacy Act.

"We will likely be filing a motion for reconsideration," Fisher's attorney Robert Charrow said to **The Cancer Letter.** Along with requesting that the three-judge panel reconsider its ruling, the motion is likely to request a rehearing by the entire court, Charrow said.

Action Plan on Breast Cancer

Panel Sets Broad Agenda For Genetic Research

A research agenda proposed recently by a working group of the National Action Plan on Breast Cancer calls for a broad-based approach to the study of genetic susceptibility to breast cancer.

The agenda proposed at a workshop of the Action Plan's Hereditary Susceptibility Working Group calls for studies in basic biology and function of the BRCA1 and BRCA2, the natural history of cancers in mutation-positive women, the genetic epidemiology of inherited breast cancer, the efficacy of prevention and treatment strategies for mutation carriers, and the psychosocial implications of disclosure of genetic information.

"An increased understanding in these areas is crucial for these advances in basic science and technology to translate into reductions in breast cancer morbidity and mortality," the research agenda states.

The agenda was produced as a result of a workshop convened by the working group headed by Francis Collins, director of the National Center for Human Genome Research, and Mary Jo Kahn, a patient activist.

The priorities identified at the workshop and included in the research agenda are more specific than the current goals of the NCI Cancer Genetics Network, the Institute's emerging program for the study of cancer risk associated with inherited generic mutations (**The Cancer Letter**, Nov. 29, 1996).

Initially, the NCI network is aiming to address the infrastructure needs of genetic testing for all cancers by setting up eight research centers as well as centers for data management and communications.

"The NCI Cancer Genetics Network is one of the mechanisms through which the the Action Plan's research objectives can be achieved," said Caryn Lerman, associate professor at Georgetown University's Lombardi Cancer Center. "Our

recommendations are intended to apply more broadly to research on hereditary breast cancer."

The final document from the Sept. 5 workshop, co-chair by Lerman and Lawrence Brody, a scientist with NCHGR, was released late last month.

The text of the research agenda follows:

Basic Science

●Collect a wide variety of biological materials from carriers of breast cancer susceptibility genes (e.g., DNA, fibroblasts, lymphoblasts, tumor and normal breast tissue, fresh and fixed). Consistent collection of these biological materials will greatly aid the development of diagnostic technologies and speed basic biological research.

●Evaluate potential adverse biological effects on carriers of radiation exposures, including mammography screening (frequency and dose), ambient and occupational exposures, and exposure to new imaging methods. The biological specimens from mutation carriers (see above) can be used to test for radiation sensitivity in vitro assays.

●Develop functional tests for the BRCA1/2 genes. Such methods would complement DNA-based diagnostics and possibly allow the interpretation of an inconclusive DNA test.

●Investigate the effects of modifier genes, such as the ataxia telangiectasia gene, on BRCA1/2 mutation carriers.

Genetic Epidemiology

●Characterize BRCA1 and BRCA2 more fully with respect to the spectrum of mutations, their prevalence (respective frequencies) and associated risks (including age-at-onset and cumulative risk). Since study design appears to be an important correlate of the characteristics observed to date, the best data to address this question will come from population-based surveys, possibly extending to family members of identified mutation carriers. Note: Feasibility of distinguishing between disease-related and neutral variants will be greatly enhanced by the availability of functional assays.

●Characterize the natural history of disease among BRCA1 and BRCA2 mutation carriers, including recurrence, survival, second primary tumors as well as the full spectrum of associated cancers. This objective requires large numbers, which can only be achieved through coordination across multiple sources (studies, institutions, etc.), possibly through the development of a registry.

●Determine factors that influence penetrance and prognosis among BRCA1 and BRCA2 mutation carriers. These potentially include other genes (e.g., HRAS1 VNTR), lifestyle behaviors and environmental exposures (e.g., exogenous hormones), and therapeutic options (e.g., various chemotherapeutic regimens).

●Identify other breast cancer susceptibility genes. Research on genetic polymorphisms that affect metabolism of drugs, hormones, and carcinogens may be considered a higher priority than research directed at high-risk families unlinked to BRCA1/2, because of the potential impact of lower penetrance but high frequency alleles on breast cancer in the general population.

Prevention and Treatment

●Identify biomarkers as surrogate correlates of tumor incidence and long-term survival. This could lead to model systems for more rapid evaluation of prevention strategies.

●Develop and evaluate improved breast cancer surveillance strategies, including better imaging techniques and mammography.

●Evaluate the efficacy among BRCA1/BRCA2 mutation carriers of potential public health and medical interventions designed for early detection and prevention, e.g., mammography screening (especially in younger women), prophylactic surgeries, and chemoprevention.

●Evaluate the safety and efficacy of breast-conserving therapies versus mastectomy (unilateral and bilateral) in women affected with hereditary forms of breast cancer.

Psychosocial Research

●Evaluate the impact of genetic testing in newly identified high risk individuals and identify predictors of positive and adverse outcomes. Key outcome variables include comprehension of genetic information, quality of life (i.e., financial, emotional, sexual and family functioning), and health and lifestyle behaviors.

●Evaluate the relative effectiveness of alternate strategies for genetics education and counseling (e.g., length of counseling follow-up), alternate settings (e.g., primary care, cancer center), and alternate providers of counseling (e.g., nurses, genetic counselors, physicians).

• Evaluate the benefits of psychosocial interventions provided as adjuncts to standard genetic counseling.

• Evaluate the cost-effectiveness of genetic testing. Data on costs of counseling and testing, downstream costs, and health effects could be collected to model the cost-effectiveness of alternate counseling approaches and medical interventions in population subgroups.

Upcoming Cancer Meetings

January

AACR/ASCO Joint Conference: Basic and Clinical Aspects of Lymphoma—Jan. 10-14, Palm Springs, CA. Contact AACR, tel: 215-440-9300, fax: 215-440-9313.

Dimensions in End-of-Life Care Teleconference—Jan. 16, noon-1:15pm EST. Other dates Jan. 30 and Feb. 20. Contact Cancer Care Inc., tel: 1-800-813-4673 or 212-302-2400.

Arizona Cancer Center 7th International Workshop on Chromosomes in Solid Tumors—Jan. 20-22, Tucson, AZ. Contact Patty Sundberg, tel: 520-626-2276, fax: 520-626-2284.

Marrow Transplantation in Children: Current Results and Controversies—Jan. 23-25, Ft. Lauderdale, FL. Contact Dr. Michael Trigg, Univ. of Iowa, tel: 319-356-1608, fax: 319-356-7659.

***National* Conference on Cancer Nursing Research**—Jan. 23-25, Panama City, FL. Contact American Cancer Society, tel: 404-329-7616.

February

Second Annual Cancer Information Exchange—Feb. 13-16, Amelia Island Plantation, FL. Contact Columbus Community Clinical Oncology Program, Adina Cook, tel: 614-443-2267, fax: 614-443-5245.

American Cancer Society National Conference on State of the Art in Cancer Genetics—Feb. 20-22, Dallas, TX. Contact Iris Goodson, tel: 404-329-7604, fax: 404-329-5713.

Radiation Therapy Oncology Group Semi-Annual Meeting—Feb. 20-23, Houston, TX. Contact Nancy Smith, RTOG, tel: 215-574-3205, fax: 215-928-0153, email: nsmith@acr.org.

Molecular Advances in Cancer Epidemiology and Prevention—Feb. 20-22, San Francisco, CA. Contact UCSF CME Office, tel: 415-476-5808.

March

Basic and Clinical Aspects of Breast Cancer—March 7-12, Keystone, CO. Contact American Association for Cancer Research, tel: 215-440-9300, fax: 215-440-9313.

Supportive Care in Cancer—March 9-13, Banff, Alberta, Canada. Contact Kelli Gregg, CME director, tel: 214-820-8434, fax: 214-820-8224.

Association of Community Cancer Centers Annual Meeting—March 19-22, Washington, DC. Contact David Walls, ACCC, tel: 301-984-9496, fax: 301-770-1949.

American Society of Preventive Oncology Annual Meeting—March 23-25, New Orleans, LA. Contact Judy Bowser, ASPO, tel: 608-263-6809.

RFP Available

RFP NCI-CM-87003-28

Title: **Maintenance of a Rodent Production Center**

Deadline: Approximately March 14

The Biological Testing Branch of the Developmental Therapeutics Program, Division of Cancer Treatment, Diagnosis and Centers, NCI, is seeking an organization with the capabilities and facilities for producing pathogen-free rodents. To be considered for award of a contract, the following mandatory criteria must be met at the time of proposal submission: The offeror must have the capability to deliver in environmentally-controlled trucks to the NIH campus in Bethesda, MD, and to Frederick, MD. To be considered further for award, offerors should meet the following criteria: 1) have existing facilities which have the capability and performance records which document the successful exclusion of pathogenic organisms, 2) the principal investigator and other key personnel should have experience and expertise with rodent inbreeding procedures, and with the production of highest quality rodents, 3) organizational experience with the production of highest quality laboratory animals, and 4) willingness to participate in grantee reimbursement collections. It is expected than one cost-reimbursement completion type contract will be awarded for a five year period as a result of this solicitation. This award will be for 2,000 to 2,500 cages (mouse equivalents). All breeding stock will be supplied by the government. The strains and stocks to be produced will be determined by the government. This procurement is designated as a 100 percent small business set-aside, with a corresponding SIC# 8731.

Inquiries: Carolyn Barker, Contract Specialist, Treatment Contracts Section, Research Contracts Branch, NCI Executive Plaza South Rm 603-MSC 7220, Bethesda, MD 20892-7220, tel: 301-496-8620, fax: 301-402-6699.

Program Announcements

PA-97-019 P1O1

Title: **Aging, Race, And Ethnicity In Prostate Cancer**

The National Institute on Aging, NCI and the National Institute of Environmental Health Sciences invite research grant applications to expand the understanding of biological and clinical factors leading to the development, progression, and treatment of prostate cancer in aging men. The increased risk of prostate cancer with advancing age and its prominence in older-aged men are well known characteristics of this tumor. The unusually high incidence and mortality rates of prostate cancer for older white and black American men and, by contrast, the much lower rates in men of Hispanic and Asian descent, provide the need for research that emphasizes the role of race and ethnic factors, as well as age, in early diagnosis, management, and etiology of this tumor. This PA is intended to stimulate research that applies the expanding scientific knowledge gained on prostate cancer to older men and to extend the knowledge base on age-related aspects of the etiology of this malignancy. The mechanisms of support will be the investigator-initiated research project grant (R01) and FIRST award (R29).

Though investigators acknowledge aging as a high risk factor for prostate cancer, current studies are limited by a lack of attention to the aging process and/or old age in combination with race, and ethnic factors. Further, it is also recognized that black Americans are affected by this tumor to an even greater extent than white Americans and that men of other race or ethnic origin are affected far less. Despite these striking age, race, and ethnic differences, no extensive research focus has been directed toward the role of aging, race, and ethnicity in prostate cancer.

This PA encourages the extramural research community to take advantage of recently acquired scientific knowledge and expertise developed in biology, gerontology, oncology, urology, and other disciplines and professions and apply these resources to aging relevant research questions on prostate cancer for aging males of different races and minority backgrounds.

Major questions on prostate cancer in the context of an aging host invite multidisciplinary research in the areas of early diagnosis, management, and etiology of prostate cancer. Research efforts, single or in combination, focusing on diagnosis, management, and etiology, may be addressed as these areas pertain to aging, race, and/or ethnic groups.

The targeted areas of research relevant to this PA are identified below. These are not exclusive and related issues designated by the applicant will be considered.

Etiology and Risk Factors: Studies on factors that affect the rate of increase with age in risk for prostate cancer, and/or the rate of development and progression of premalignant changes in prostate tissue, as well as their interaction with familial factors, race, and/or ethnicity; epidemiologic studies of age-related familial, genetic, and environmental factors that may affect the age of onset, rate of progression, and duration of survival for prostate cancer; interactions of aging and age with prostate cancer risk factors (e.g., relative prominence of various risk factors for onset of prostate cancer at different ages; risk factors for occurrence of multiple primary prostate tumors.

Disease Progression: Extent to which, and mechanism by which, age-related prostate growth leads to increased incidence of prostate cancer; role of other age-related biological factors that lead to the development and affect the progression rate of prostate cancer; assessment of protective factors that mitigate against prostate cancer (allow aging without development of premalignant changes); metastatic potential of various precursor lesions for prostate cancer in aging men.

Diagnosis: Testing of improved methods to identify high risk older white and black men and low risk men of different race and ethnic origin through development of new techniques to distinguish premalignant changes from nonmalignant age-associated changes in prostate tissue; validation of new and/or current methodologies or application of current biological, physiological, and clinical techniques to identify high-risk older white and black men [e.g., prostatic intraepithelial neoplasia (PIN) and prostate-specific antigen (PSA)]; methods to distinguish older men with "clinically significant" cancer preoperatively; verification of diagnostic specificity and predictive value of PSA parameters for older men; studies of the causes of racial/ethnic disparities in disease stage at diagnosis (black men present with advanced disease stage more frequently);effects of age-associated changes on sensitivity, specificity, prognostic value of diagnostic techniques and their predictive value for response to treatment. Testing new methods and technologies to reduce age-associated problems in diagnosis and prognosis.

Management: Testing new interventions or treatment strategies in older men with comorbid conditions to reduce age-associated complications or lessen age-associated reduction in treatment efficacy (as measured by treatment outcomes such as quality of life, functional status, and/or survival experience); clinical determinants of age- and ethnicity-associated differences in prostate cancer treatment efficacy and effectiveness for such outcomes as survival, treatment complications, side effects of treatment, and functional status; factors responsible for differences among age and ethnic groups in treatment received and clinical outcomes (e.g., stage at diagnosis, presence of comorbid conditions, age selection bias by physicians) and the effects of interactions among such

factors. These may address: Special features of aging and/or symptoms of illness in old age that influence the treatment and care of older-aged prostate cancer patients and relate to treatment differences or modifications made because of old age; assessment of the effectiveness of different treatments relative to the stage of disease and characteristics of old age (e.g., poor repair mechanisms, functional loss, greater susceptibility to toxicity of treatment); evaluation of tolerance and response to standard or experimental adjuvant radiotherapy regimens or multimodality prostate cancer treatment interventions, controlling for physiologic parameters and other factors; effects of age-associated, cultural, and life-style changes on sensitivity, specificity, prognostic value, and predictive value for treatment responsiveness and diagnostic techniques; effects of previous and/or concurrent illnesses on prostate cancer treatment recommendations.

Ancillary Studies/Existing Databases: Ancillary studies conducted with the NCI Clinical Trials Research Cooperative Groups, SEER Special Studies, and population-based tumor registry studies related to aging, race, and ethnicity in prostate cancer are welcome for this research solicitation. These may include studies on barriers to recruitment of older white and black males to prostate cancer clinical trials (e.g., comorbid conditions, physical frailty, lack of transportation), quality of life parameters for cancer patient survival follow-up; analyses of existing databases applicable and relevant to addressing treatment of older prostate cancer patients. Emphasis on older ethnic populations that may be compared with white and black populations is encouraged (e.g., longitudinal studies such as the Baltimore Longitudinal Study on Aging; Normative Aging Study; Framingham Study; as well as clinical studies). Research applications require a thorough and detailed explanation of the data elements in the studies identified as candidates for this research solicitation. Special attention should be given to ascertaining biases in the databases.

Inquiries: Rosemary Yancik, Geriatrics Program, National Institute on Aging, Building 31, Room 5C05, Bethesda, MD 20892, tel: 301/496-5278, fax: 301/496-2793, email: YancikR@31.nia.nih.gov.

Andrew Chiarodo, Organs System Coordinating Branch, NCI, Executive Plaza North, Room 512, Bethesda, MD 20892, tel: 301/496-8528, fax: 301/402-0181, email: ac53a@nih.gov

Gwen Collman, Division of Extramural Research and Training, National Institute of Environmental Health Sciences, PO Box 12233, Research Triangle Park, NC 27709, tel: 919/541-4980, fax: 919/541-4937, email: collman@niehs.nih.gov

PAR-97-021 P1O1
Title: **High-Throughput Technologies To Detect Alterations In Tumors**

The Technology Development Branch of the Cancer Diagnosis Program, Division of Cancer Treatment, Diagnosis and Centers, NCI, invites Program Project grant applications (P01s) proposing the development of high-throughput technologies for the evaluation of the spectrum of molecular alterations in primary tumor tissue. The P01 funding mechanism is being used to facilitate collaborations between researchers developing novel technologies and clinical investigators with the appropriate expertise and resources to assess the application of the technologies to tumor specimens.

Applicants may request up to $750,000 per year direct cost, however, each budget item must be carefully justified. The period of support may be for up to five years. This PA will be in effect for two years, up to and including the October 1, 1998, P01 receipt.

This initiative invites grant applications to support development of high-throughput technologies for analysis of the spectrum of molecular alterations in primary tumor tissues. The applications should propose development of appropriate technologies and studies to assess their use in analysis of primary tumor specimens. Modification of these technologies to optimize their utility in the clinical setting may also be proposed. Technologies may be designed to analyze a variety of alterations including genome-wide cytogenetic changes; mutations in constellations of genes known to be important in tumor initiation and progression, including genes that are members of pathways of cellular regulation; analysis of all possible mutations in a single gene; changes in patterns of gene expression at the level of both RNA and protein; or changes in protein function. The applications must document access to appropriate tumor tissue resources to facilitate evaluation of the technologies in clinical specimens. Development of informatics systems to support collection and evaluation of research data may also be proposed.

This program encourages interactions among academic scientists and clinicians, basic scientists involved in the development of new technologies and informatics specialists. The initiative envisions collaborations among commercial or academic organizations with appropriate programs in technology development and academic institutions with expertise and ongoing programs in cancer biology and genetics with the necessary clinical resources. These collaborations will ensure that the technologies developed are appropriate steps toward meeting the clinical needs of the cancer community.

Inquiries: James Jacobson, Division of Cancer Treatment, Diagnosis and Centers, NCI, 6130 Executive Boulevard, Room 513, MSC 7388, Bethesda, MD 20892-7388, tel: 301/496-1591, fax: 301/402-1037, email: JJ37D@NIH.GOV