THE CANCER LETTER INTERACTIVE

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Kidney, Bladder Cancer Causes, Treatment Need More Research, NCI Advisors Find

NCI should fund more research to develop a greater understanding of the biological mechanisms underlying the risk factors for kidney and bladder cancers, an advisory group formed to review NCI's kidney and bladder cancer programs concluded.

In a report accepted July 10 by the Advisory Committee to the NCI Director, the Kidney/Bladder Cancers Progress Review Group said it had identified 13 research priorities that, if funded by NCI, could eventually improve the prevention and treatment of these diseases.

"Although research has shed some light on the environmental and genetic origins of kidney and bladder cancers, this knowledge has yet to be translated into significant reductions in the burden of these diseases,"

(Continued to page 2)

In Brief:

Trapido To Lead NCI's Epidemiology Program In DCCPS; MSK Plans Bioinformatics Research

EDWARD TRAPIDO, of the University of Miami School of Medicine, was appointed associate director of the Epidemiology and Genetics Research Program in the NCI Division of Cancer Control and Population Sciences. Trapido will plan, direct, and manage NCI's extramural epidemiology and genetic epidemiology research program, which supports more than 400 research grants and cooperative agreements totaling $280 million. He will join NCI in September. Trapido is professor and vice chairman of the Department of Epidemiology and Public Health, University of Miami School of Medicine. He also is associate director for cancer prevention and control at the Sylvester Comprehensive Cancer Center, and directs the M.P.H. and Ph.D. Epidemiology Teaching Programs. Trapido serves as principal investigator of several cancer control research and education programs, including the NCI Cancer Information Service, Florida Cancer Data System, Florida Comprehensive Cancer Control Initiative, and the Southeast Region of Redes En Action, which focuses on Hispanic cancer prevention and control activities. He also is director of the Tobacco Research and Evaluation Coordinating Center and special consultant to the Florida Tobacco Pilot Program. Before joining the University of Miami in 1984, Trapido was a staff fellow for three years in NCI's intramural epidemiology program. **Deborah Winn** is the acting associate director of EGRP. . . . **COMPUTATIONAL BIOLOGY CENTER** at Memorial Sloan-Kettering Cancer Center has begun a major initiative to develop computational methods in basic biology

(Continued to page 8)

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Kidney, Bladder PRG Report Lists 13 Priorities For Research

(Continued from page 1)

the report said. "At present, mortality from kidney and bladder cancers is high and survival is low. Techniques for early diagnosis of these cancers are extremely limited and treatment fails in 95 percent of patients with advanced disease. Only greatly intensified research efforts across the disease continuum will change the currently bleak outlook for most individuals afflicted with these cancers."

Kidney and bladder cancers account for about 88,300 cancer cases and 24,200 deaths per year in the U.S., nearly 7 percent of all cancer cases and more than 4 percent of all cancer deaths, the report said. The two cancers account for nearly 10 percent of all cancers in men and more than 4 percent of all cancers in women.

Black men have higher incidence and mortality rates for kidney cancer, and higher mortality rates for bladder cancer, than white men.

Kidney cancer incidence has been increasing at a rate of about 2 percent per year for the past 65 years. The reasons for this increase are unclear. The incidence of bladder cancer is declining at just under 1 percent per year.

The full text of the report is available at http://prg.nci.nih.gov/kidney/finalreport.html.

Excerpts of the report follow:

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Introduction

The first known cause of human bladder cancer was occupational exposure to certain members of a class of chemical compounds known as the arylamines, which include 2-naphthylamine, 4-aminobiphenyl, and benzidine. Another well-established risk factor is cigarette smoking, which accounts for an estimated 50 percent of all bladder cancers diagnosed in the United States today. The length of time between carcinogen exposure and development of bladder cancer can be 20 years or more.

Experimental data also point to the involvement of the enzyme cyclooxygenase-2 in bladder cancer development. A recent U.S. study reports a statistically significant reduction in the risk of bladder cancer among regular, long-term users of nonsteroidal anti-inflammatory drugs, which inhibit the expression of cyclooxygenase-2. Further research is needed to validate this finding and delineate its clinical significance.

Considerable experimental and epidemiologic data have established *S. haematobium* (schistosomiasis) as a causal agent of human bladder cancer, specifically squamous cell cancer. Schistosomiasis is hyperendemic in Egypt and parts of the Middle East, where bladder cancer is among the top three most frequently diagnosed cancers.

Finally, epidemiologic studies have suggested a 20 to 100 percent increase in bladder cancer risk among subjects in the highest category of long-term exposure to chlorinated surface water compared with those with no such exposure. Water consumption appears to exert a protective effect: a 1999 study found that men drinking six or more 8-oz cups of water per day halved their risk of bladder cancer compared with men who drank less than one cup of water per day.

For both renal cell carcinoma and cancer of the renal pelvis, cigarette smoking is a well-established risk factor. Phenacetin, a major ingredient of analgesics until about two decades ago when it was banned from all drugs manufactured in the United States, is a recognized causal factor for cancer of the renal pelvis. For renal cell carcinoma, several recent large-scale epidemiologic studies have confirmed obesity and hypertension as two independent, major risk factors. Some data suggest that trichloroethylene exposure is a risk factor for renal cell carcinoma. People with end-stage renal disease also are at increased risk for kidney cancer.

In spite of significant numbers of studies, however, the etiology of most kidney cancers is unclear.

Overall, the etiological mechanisms of kidney and bladder cancers remain poorly understood. Better elucidation of these mechanisms may lead to much-needed new treatments, diagnostic methods, and prevention strategies for these diseases.

In the U.S., bladder cancer mortality varies by region and is highest in the Northeast. Most bladder cancers in the Western world are transitional cell carcinomas; this tumor type was the focus of the PRG's deliberations. Outside the U.S., patterns of bladder cancer incidence, pathology, and mortality are different; squamous cell carcinoma is the prominent histological type. Although kidney cancer has a less geographically distinct fingerprint than bladder cancer, risk does seem to be associated with higher socioeconomic status and higher mortality rates are seen in many areas of the midwestern United States.

Renal cell carcinoma accounts for 80 to 85 percent of all kidney cancers in the U.S. The remaining kidney cancers are mostly cancers of the renal pelvis (including the ureter). Kidney cancer is most commonly sporadic, but it can also be hereditary. Six clinically distinct types of inherited kidney cancer have been identified thus far, von Hippel-Lindau syndrome being the best characterized. VHL—an autosomal dominant syndrome in which kidney cancer arises from multiple benign renal cysts—occurs in 1 of every 36,000 live births, and kidney cancer occurs in 28 to 45 percent of VHL-affected individuals. Benign cystic VHL-associated tumors can also develop in the spine, brain, eye, pancreas, inner ear, and adrenal gland. Certain VHL kindreds also develop pheochromocytomas.

Research on the pathobiology of *VHL* mutations is expanding our knowledge of kidney cancer, although much work remains to be done. It is known that clear-cell carcinoma has a high degree of vascularity and that *VHL* mutations occur in 70 percent of sporadic cases of kidney cancer. The wild-type VHL protein normally forms a complex that causes the degradation of hypoxia-inducible factor-alpha (HIFa), a transcription factor that regulates a number of genes involved in angiogenesis and cell growth. Mutations in the *VHL* gene variably affect the ability of the protein to form the repressive complex, resulting in an overproduction of vascular endothelial growth factor (VEGF), Glut-1, and platelet-derived growth factor. However, links have not been established between these various molecular changes and clinical behavior. This is one of many promising areas of discovery research in which additional efforts may lead to significant advances.

Approximately 30 percent of kidney cancers are incidentally detected because of widespread and increasing use of computed tomography for other medical indications. Advances in imaging—such as CT, magnetic resonance imaging and positron emission tomography—are allowing diagnosis of malignancy at earlier stages. However, no population-based kidney cancer screening studies using CT have been conducted, nor have correlations of imaging patterns with molecular and clinical behavior been performed.

Unlike kidney cancer, bladder cancer does not have a substantial number of hereditary forms. However, the ready accessibility of the bladder to repeated cystoscopic examinations and biopsies has improved our understanding of bladder cancer biology. Alterations in the genes coding for p53, p14, p16, Rb, and cyclin D—among others—have been noted, and many bladder cancers are missing arms of chromosomes 9 and 17. Overexpression of the epidermal growth factor family of receptors is common. The patterns of gene alterations in low-grade papillary tumors are markedly different from those in more aggressive disease. Correlations between molecular and clinical phenotypes have been inconsistently and infrequently performed, suggesting that future research will bring major opportunities to improve the management of bladder cancer.

The primary treatment modalities for localized bladder cancer are transurethral resection and cystectomy; other options include intravesical chemotherapy and immunotherapy. Adjuvant chemotherapy for poor-risk localized disease has a controversial history but now appears to improve survival. In localized kidney cancer, radical nephrectomy remains the standard of care, but minimally invasive and nephron-sparing surgical techniques are becoming widely used. Early successes with radiofrequency and cryosurgical ablation of small kidney cancers are being reported.

Treatment options for metastatic bladder and kidney cancers are few and largely ineffective. Although newer compounds such as gemcitabine and the taxanes seem to lessen toxicity in the treatment of metastatic bladder cancer, they have not improved median survival. Highly toxic interleukin-2, the only approved treatment for metastatic kidney cancer, likewise has not improved median survival. Many

other therapies are being studied, including anti-vascular endothelial growth factor, anti-endothelial growth factor receptor, vaccines, cytokines, and activated T-cells, but none has yet had a major impact on the natural history of these diseases. New prognostic molecular markers are needed that may eventually allow individually targeted therapy.

The recurrence rate for bladder cancer is 80 percent; it is estimated that nearly 400,000 individuals in the U.S. are at risk for recurrence. Chemoprevention trials in this population are sorely needed; the recent data on a possible protective effect of NSAIDs on bladder cancer incidence should provide an impetus for additional research in this area. There is some evidence that earlier detection leads to better outcomes in kidney cancer, although few screening studies have been conducted. More research is needed to apply new knowledge about the molecular origins of kidney cancer to the identification of biomarkers for this disease.

Despite the severe limitations of existing therapies for kidney and bladder cancers, the number of survivors of these diseases is increasing. Factors influencing quality of life in these people are largely uninvestigated. Furthermore, disparities in incidence and mortality suggest that state-of-the-art care, with all its limitations, is out of reach for many individuals with kidney and bladder cancers. As we endeavor to develop new therapies that will extend patients' lives and lessen the burden of these diseases, it is equally important to conduct research aimed at strengthening health care delivery and improving quality of life.

Research Priorities

The 13 priorities identified by the Kidney/Bladder Cancers PRG will stimulate multidisciplinary research that can significantly advance progress against kidney and bladder cancers. The priorities, with a summary rationale for each, are as follows:

Discovery

Priority 1: ***Understand the biological mechanisms underlying the risk factors for kidney and bladder cancer phenotypes.***

Rationale: The etiological mechanisms of distinct phenotypes of renal and bladder cancer are poorly understood. Novel prevention and treatment strategies may result from improved understanding of such mechanisms.

Priority 2: ***Identify global genetic, epigenetic, RNA expression, and proteomic alterations in tumors and place them in specific biological pathways that are essential to development, progression, response to therapy, and maintenance of subtypes of bladder and kidney cancers.***

Rationale: Bladder and kidney tumors are heterogeneous in their histology and clinical behavior. Individual tumors show alterations in specific molecular pathways, potentially allowing customized clinical management for the individual patient. Understanding of the relevant growth and signaling pathways will allow the development of targeted therapies, including the use of small molecules produced through combinatorial chemistry.

Priority 3: ***Understand the role of stroma and intercellular signaling in organogenesis, tumor development, and maintenance of malignant phenotypes in bladder and kidney cancers.***

Rationale: Stromal elements are known to influence epithelial differentiation in the bladder and kidney. The tissue microenvironment—including the extracellular matrix, stromal cell complement, inflammatory cells, and local immune response–may play a role in tumor development and growth. Most studies to date have examined only the characteristics of the tumor epithelial cells.

Priority 4: ***Generate and characterize transgenic models, including conditional knock-out and knock-in strategies and orthotopic models, of bladder and kidney cancer, focusing on the use of tissue-specific promoters and targeting human disease-related genetic events. These models will allow identification and validation of prognostic, preventive, and therapeutic targets and their inhibiting agents.***

Rationale: Transgenic model systems will allow understanding of gene function, dissecting of molecular pathways, and generation of faithful models of human cancer and will also provide targets for drug discovery and chemoprevention. However, kidney and bladder cancers lag behind other organ systems in the development and utilization of these models.

Translational Research

Priority 5*: Examine blood, urine, premalignant, and tumor tissue before prevention and therapy trials to identify and quantify disease and identify targets for therapy and predictors and mechanisms of response, resistance,*

progression, and relapse.

Rationale: New anti-apoptotic and tumor-growth and inhibition molecular pathways have been identified that may influence the response to therapy in kidney and bladder cancers. The discovery of alterations in specific molecular pathways in these diseases should also facilitate the identification of molecular markers that would enable selection of appropriate patients for therapy, monitoring of the effectiveness of therapy in an individual patient, and testing of therapies in a patient population with a lower tumor burden.

Priority 6: ***Facilitate the development and utilization of noninvasive or minimally invasive techniques to image and assess the biological and clinical effects of targeted therapeutics.***

Rationale: Because kidney and metastatic bladder tumors cannot easily be sampled during therapy, noninvasive and minimally invasive methods are needed to assess therapeutic effectiveness. It will also be important to identify surrogate markers of biological effectiveness in readily accessible tissues and to identify blood and urine markers of tumor burden that will enable better assessments of treatment efficacy.

Priority 7: ***Identify and prioritize agents—alone or in combination—that target known cancer growth and progression pathways.***

Rationale: Recent studies in chronic myelogenous leukemia and gastrointestinal stromal tumors have provided proof of principle that strategies developed to target cancer gene pathways can have an effect in human tumors. Several targets are available from known cancer genes involved in the early development of several types of genitourinary cancer. Validation of the roles and therapeutic potential of agents that block these cancer gene pathways is urgently needed.

Treatment

Priority 8*: Develop innovative therapeutic strategies that will eradicate disease, preserve organ function, and maintain quality of life, using mechanism-based agents_that take into account known prognostic variables, molecular characteristics of tumors, assays of targeted effects, surrogate markers of efficacy, and novel delivery strategies.*

Rationale: Few patients with kidney and bladder cancers can be cured by existing therapies. New agents targeting specific disease mechanisms are being identified in preclinical and correlative studies. Future clinical trials need to optimally investigate both the clinical and biologic effects of these agents in clearly defined and selected patient populations.

Priority 9: ***Develop and improve approaches to risk assessment of localized and advanced disease—which take into account known prognostic variables, including stage, histology, and novel molecular factors—to direct therapy.***

Rationale: Kidney and bladder cancers are biologically heterogeneous diseases. It is clear that many patients with localized disease can be managed with less invasive therapy whereas others need more aggressive therapy. Similarly, patients with advanced disease have disparate characteristics that affect therapeutic outcomes. Better predictors of behavior and response are needed to more appropriately guide treatment of the individual patient and predict prognosis.

Priority 10: ***Develop evidence-based, hypothesis-driven research efforts in palliative care for patients with advanced kidney and bladder cancers.***

Rationale: Therapy fails in 95 percent of patients with advanced kidney and bladder cancers. In both of these tumor types, the distribution of symptom clusters in advanced disease is relatively unknown and the prognostic significance and impacts on quality of life of these symptom clusters are not well studied. For example, it would be useful to evaluate different strategies for managing bone metastases and the effects of these different strategies on mobility, function, and pain.

Cancer Control

Priority 11: ***Describe the impact of kidney and bladder cancers and their treatment on the quality of life of individuals and their families throughout the cancer continuum and develop and assess interventions that will reduce morbidity and improve health-related quality of life outcomes.***

Rationale: Although cure or increased life expectancy is a goal of medical treatment, patients and those who care for them agree that improving the quality of that life is also a high priority. Understanding the factors that affect quality of life is a prerequisite for patient-oriented treatment decision-making.

Priority 12: ***Identify, characterize, and validate molecular markers to determine the risk of disease, enhance early detection, and predict***

response to chemoprevention with new chemopreventive agents and strategies, employing new models as appropriate.

Rationale: Molecular markers can be used to select high-risk subjects for screening, resulting in more statistically powerful screening studies with smaller numbers of subjects than could be obtained by general population screening. Studies of unique populations such as young adults with bladder cancer, patients with end-stage renal disease, and post-treatment cancer patients who continue to smoke are likely to yield insights into risk factors for kidney and bladder cancers. Additionally, preclinical, mathematical, and other models are essential to the development and testing of successful, cost-effective screening and prevention strategies.

Priority 13: ***Identify and explore the gaps between and barriers to standards of practice and care that currently result in disparate outcomes for kidney and bladder cancer patients.***

Rationale: Delay in treatment appears to be correlated with a disproportionately higher death rate among women with bladder cancer, who are diagnosed 6 to 9 months later than men. Black men have a higher mortality rate for both bladder and kidney cancers than white men. Once the causes of these and other apparent disparities in health care delivery are understood, strategies can be devised to remedy them.

Resources Needed

The PRG also identified resources that will be needed to achieve the above priorities:

—Animal and cell-based models.

—Large, multifaceted studies (epidemiologic, treatment, chemoprevention) conducted with international collaboration. These studies should include quality-of-life endpoints, have standardized consent forms, and include comprehensive and longitudinal sampling of tumor, urine, and blood. Adequate infrastructure is necessary for these trials to be successful.

—Specimen banks (tumors, normal tissue, blood, urine, etc.) available to all investigators.

—Standardization of common data elements and assays, with clinical validation.

—Validated, high-quality high-throughput technologies for the analysis of DNA, RNA, and protein in tumors.

—Bioinformatics and biostatistical approaches for clinical trial analysis.

—Resources, primarily through industry, to produce and screen small molecules to target tissue-specific growth and signaling pathways. (This effort will require close cooperation between academia and industry.)

—A patient advocacy group in bladder cancer, modeled after the kidney cancer advocacy group, which will help to establish research priorities at the national level and can advocate for scientific studies and clinical trials.

—Noninvasive imaging modalities to evaluate therapeutic efficacy in vivo.

—Suitable targets for testing in humans and agents capable of affecting those targets.

—Training of young investigators focused on kidney and bladder cancers.

—Centers and networks of disease-specific clinical research, which could include expanding the definition of the Specialized Programs of Research Excellence (SPOREs) to encourage multi-institutional consortia.

—A centralized database management system for patients participating in clinical trials sponsored by the National Cancer Institute, cooperative groups, and the pharmaceutical industry, as well as for patients in investigator- or institution-initiated pilot trials.

—Training for physicians, nurses, and other providers in quality-of-life assessment and data utilization.

—Linking large databases such as SEER and Medicare to improve our understanding of practice patterns that may create gaps in and barriers to the care of patients with kidney and bladder cancers.

—Multimedia modalities and collaborative community outreach activities to enhance the provider-patient relationship.

Panel Calls For More Attention To Pain, Fatigue, Depression

Health-care professionals and researchers need to pay greater attention to the pain, fatigue, and depression that cancer patients commonly experience, a panel advising NIH said July 17.

Despite effective interventions, cancer pain is often under treated, the panel said following the NIH State-of-the-Science Conference on Symptom Management in Cancer. Cancer-related depression and fatigue are less clearly defined, but are common and have a profound impact on patients' well-being.

More resources need to be devoted to studying the occurrence, causes, and impediments to effective treatments of these symptoms, the panel said.

"Currently, cancer-related pain, depression, and fatigue are under treated and this situation is simply unacceptable—there are effective strategies to manage these symptoms and all patients should have optimal symptom control," said panel chairman Donald Patrick, professor and director of the Social and Behavioral Research Program in Public Health at the University of Washington in Seattle.

Despite advances in early detection and effective treatment, cancer remains one of the most feared diseases, not only because of its association with death, but with diminished quality of life, the panel said. While research is producing new insights into the causes and cures of cancer, efforts to manage the symptoms of the disease and its treatments have not kept pace. Addressing the total quality of life of cancer patients, including the effective management of symptoms, is an increasingly critical aspect of efforts to reduce the burden of cancer.

The panel members found that the available evidence supports a variety of interventions for treating cancer patients' pain, depression, and fatigue. The panel noted numerous factors that can interfere with adequate symptom management, including: incomplete effectiveness of some treatments; a lack of sufficient knowledge regarding effective treatment strategies; patient reluctance to report symptoms to caregivers; a belief that such symptoms are simply a part of the cancer experience that must be tolerated; and inadequate coverage and reimbursement for some treatments.

The panel pointed out the additional difficulty presented by the interactions among these three symptoms. For example, a successful treatment for depression might also alleviate fatigue, but conversely, adequate pain management may exacerbate fatigue.

The panel's statement concluded that:

—clinicians should use brief assessment tools routinely to ask patients about pain, depression, and fatigue and to initiate evidence-based treatments;

—current evidence to support the concept of cancer symptom clusters is insufficient, and additional theoretically driven research is warranted;

—research is needed on the definition, occurrence, treatment of pain, depression, and fatigue alone and together in adequately funded prospective studies;

—all patients with cancer should have optimal symptom control from diagnosis throughout the course of illness, irrespective of personal and cultural characteristics.

Among the evidence considered by the was a report prepared by the New England Medical Center Evidence-based Practice Center under contract to the Agency for Healthcare Research and Quality. A summary of the Evidence Report on Management of Cancer Symptoms: Pain, Depression, and Fatigue is available at http://www.ahrq.gov/clinic/epcix.htm. Copies are also available from the AHRQ Publications Clearinghouse, phone 800-358-9295. The National Library of Medicine prepared a bibliography on this topic, available at http://consensus.nih.gov.

The full text of the panel's statement is available in draft form at http://consensus.nih.gov.

Cancer Centers:

Mayo Wins NCI Designation For Its Entire Cancer Program

Mayo Clinic's designation as an NCI comprehensive cancer center in Rochester, Minn., has been extended to include Mayo's locations in Scottsdale, Ariz., and Jacksonville, Fla.

The extended designation makes Mayo Clinic the first multicenter institution in the U.S. to receive comprehensive cancer center designation for its entire cancer program. The designation followed an endorsement by NCI of plans by Mayo Clinic to reorganize the cancer research, treatment, and education programs at its three locations into a single cancer center.

"We fully agree (with) the reorganization of the Mayo Clinic Comprehensive Cancer Center that established a foundation-wide cancer center encompassing the Jacksonville and Scottsdale sites," said Brian Kimes, director of the NCI Office of Centers, Training and Resources. "We believe that the benefits that will accrue to cancer research and cancer patients will be substantial."

This year an estimated 13,000 new cancer patients will seek treatment at Mayo Clinic.

"A Mayo Clinic Comprehensive Cancer Center in three locations will further ensure our goal that patients with cancer will receive the same standard of treatment regardless which Mayo Clinic location they choose for their care," said Hugh Smith, chairman of the Board of Governors at Mayo Clinic in Rochester. "It also will enable us to better coordinate our current research programs and to expand our

future research endeavors into the emerging sciences such as genomics."

For Scottsdale, the designation gives patients the choice of coming to the only NCI-designated cancer center in that region where they will have full access to clinical trials and other research and treatment programs that connote a comprehensive cancer center, according to Victor Trastek, chairman of the Board of Governors at Mayo Clinic in Scottsdale.

In Jacksonville, researchers are being recruited to run the research programs that will be housed in the new C.V. and Elsie R. Griffin Cancer Research Building. Planning has begun to expand cancer treatment programs for patients, said Denis Cortese, chairman of the Board of Governors at Mayo Clinic in Jacksonville.

Franklyn Prendergast, director of the Mayo Clinic Comprehensive Cancer Center, said the NCI designation is the culmination of more than four years of planning and formally establishes one Mayo Clinic Comprehensive Cancer Center with three doors of entry.

"Currently, the majority of cancer research and patient treatment occurs in Rochester," said Prendergast. "We will maintain the reputation that Rochester has established in research and treatment while further developing areas of research and treatment in Scottsdale and Jacksonville."

Mayo Clinic recently approved expansion plans for the cancer center and its research programs in all three of its locations:

—Jacksonville: The Griffin Cancer Research Building will provide 40,000 square feet of new laboratory space for cancer researchers. Five new researchers will be recruited, including a deputy director for the cancer center and research programs.

—Rochester: Cancer research laboratories will expand into 35,000 square feet of new laboratory space in the recently constructed Gonda Building, and 12 new researchers will be recruited.

—Scottsdale: Three new cancer researchers will be recruited this year, and plans will be developed to build additional research facilities. Laurence Miller will become the new deputy director of the cancer center and research programs on Aug. 1. Along with treating patients, Miller will continue his research on pancreatic cancer in Scottsdale.

The single cancer center will enable Mayo Clinic to more cohesively expand its cancer prevention and treatment programs to minority and underserved populations, Prendergast said.

In Brief:

Chris Sander Joins MSKCC's Computational Biology Center

(Continued from page 1)

and cancer research and to obtain medical knowledge from the human genome. **Chris Sander**, computational biologist and executive editor of Bioinformatics, has joined the center. "Chris Sander's expertise in analyzing protein structures and genomic information, and his work to represent biological pathways in computational form and simulate the behavior of molecules, cells, and organs accurately on computers, will help us deliver on the promise of the Human Genome Project," said **Harold Varmus**, president of MSKCC. . . . **AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY** has named the recipients for the ASTRO Gold Medal Award for their contributions to radiation oncology. The awardees are: **Steven Leibel,** of Memorial Sloan-Kettering Cancer Center, **Victor Marcial**, of the University of Puerto Rico School of Medicine and University Hospital in San Juan, and **Marvin Rotman,** of SUNY Downstate Medical Center in Brooklyn. The award will be presented Oct. 8, during the ASTRO annual meeting in New Orleans. . . . **LYMPHOMA RESEARCH FOUNDATION** has named four individuals to its scientific advisory board: **Richard Ambinder**, director, Division of Hematologic Malignancies, Department of Oncology, Johns Hopkins School of Medicine and program leader of the Viral Oncology Program, Sidney Kimmel Comprehensive Cancer Center; **Arnold Freedman**, associate professor of Medicine, Harvard Medical School, Dana-Farber Cancer Institute; **Elaine Jaffe**, chief, Hematopathology Section, Laboratory of Pathology, NCI; and **Sharon Murphy**, chief, Division of Hematology/Oncology, Children's Memorial Hospital, Northwestern University Medical School. **Joseph Bertino** is chairman of the board. . . . **PETER HOLT**, senior scientist with the American Health Foundation, has received the Janssen Lifetime Achievement Award in Digestive Sciences from the American Gastroenterological Association. Holt received the award, sponsored by Janssen Pharmaceutical Co., during Digestive Diseases Week, May 19-22 in San Francisco. Holt, whose research has involved carcinogenesis and chemoprevention, plans to develop a translational research program for colorectal cancer prevention.

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