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Interleukins Power Immune Reaction to Metastatic Cancer

New results from NCI's Center for Cancer Research (CCR), reported in the November 15 *Cancer Research*, show promise for interleukins (IL) to enhance the body's natural ability to fight cancer that has spread to the liver. A combination of IL-12 and IL-18 increased the concentration of natural killer (NK) cells in animals and triggered therapeutic levels of interferon-gamma (IFN-γ), a key messenger molecule that regulates the immune system defenses against cancer in the liver, a common site of tumor metastasis.

NK cells are key players in the immune process, and are aptly named because they act like commandos on a search-and-destroy mission for virally infected and cancerous cells.

"This combination of interleukins significantly modifies the microenvironment in the liver and has potent antitumor activity," said Dr. Robert H. Wiltrout, director of CCR and head of the lab where the work was done. "Immunotherapeutic approaches using this strategy represent a novel approach to treating tumors in the liver." Current treatments to surgically

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Director's Update

Guest Director's Update by Dr. Malcolm Smith

Initiative TARGETs Childhood Cancer

Dr. Malcolm Smith, Associate Branch Chief for Pediatrics, Cancer Therapy Evaluation Program, NCI

Although there has been an explosion in the development of molecularly targeted therapies, these advances have been largely limited to the treatment of adult cancers. The need for new treatment approaches for childhood cancers, however, is substantial. The dramatic improvements in outcome seen over the last several decades have slowed, and, in many cases, current treatment approaches for childhood cancers cause serious short- and long-term side effects.

To see that children do benefit from advances in molecularly targeted cancer therapeutics development, NCI and the Foundation for the National Institutes of Health (FNIH) have established the Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments, or TARGET, Initiative.

The TARGET Initiative is a public-private partnership to identify and

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(Interleukins continued from page 1)
resect or transplant the liver are only effective in a minority of patients.

Interleukins and other cytokines occur naturally in the body as signaling molecules, which are part of the immune system, but they may also be reproduced in recombinant form in the lab. "We knew that both IL-12 and IL-18 each ramp up NK cell production separately, but now we find that when given together, they have a synergistic effect," said Jeff Subleski of CCR, lead author.

The combination of IL-12 and IL-18 not only increased the number of NK cells, but also continued to populate the liver microenvironment and mediate IFN-γ for at least 2 weeks. Previous work with each interleukin alone had shown the IFN-γ effect to drop significantly within 4 days or less. "This means that IFN-γ appears to play a key role in triggering immune cells to attack cancer cells," said Mr. Subleski.

The key to sustaining high levels of IFN-γ, noted Dr. Wiltrout, was turning down the number of natural killer T (NK-T) cells, another immune system operative. Even though NK-T cells in the liver similarly increase IFN-γ, they also can suppress antitumor immune system activity, he explained.

"NK-T cells are heavily expressed in the liver because it is the junction between the blood stream and the gut where foreign antigens and bacteria are common, and where initial immune defenses are strategically effective. But NK-T cells may also serve as sentinels by initially suppressing immune reactions that would be excessive," said Dr. Wiltrout.

He further explained, "You don't want immunosuppression to contribute to tumor spread or progression." In this experiment, the novel combination of IL-12 and IL-18 reduced the regional NK-T cell population to undetectable levels before they could suppress the IFN-γ impact on the tumors.

Initiation of an immune response against a tumor requires a complex set of events. Information gained from animal studies will likely provide insight into how the power of the immune system can be harnessed to develop new anticancer therapies.

"These are very promising findings for the immunotherapy of any type of cancer that is sensitive to killing by NK cells, as it does not require identification of molecules unique to the tumor," said Dr. Jay A. Berzofsky, chief of CCR's Vaccine Branch. "By diminishing the suppressive effects of NK-T cells, the IL-12/IL-18 combination treatment could provide a one-two punch needed to immunologically control cancer." ◆

By Addison Greenwood

(Director's Update continued from page 1)
validate therapeutic targets so that new, more effective treatments can be developed for children with cancer. Its immediate goal is to make major advances in identifying and validating therapeutic targets for two or more childhood cancers within 2 years of project initiation. FNIH will raise money from the private sector to augment NCI resources allotted for the initiative.

TARGET builds upon a workshop sponsored by NCI and the American Cancer Society in May 2005 that brought together scientists, advocates, and foundation and industry representatives to discuss the challenges in identifying effective new treatment approaches for children with cancer. It also builds upon the experience and expertise NCI has gained in working with the National Human Genome Research Institute to develop The Cancer Genome Atlas (TCGA) Pilot Project.

TARGET will have three primary areas of research focus. The first involves high-throughput array-based technologies to comprehensively characterize genomic and transcriptomic profiles for selected childhood cancers. The second will utilize gene resequencing to identify genes that are consistently altered in specific childhood cancers, as these genes represent strong candidates for therapeutic targeting. Finally, high-throughput RNA interference and small-molecule screening methods will be applied to identify and validate therapeutic targets.

A key principle in implementing this initiative is to leverage the investments NCI has already made in other programs and initiatives, including TCGA, the Strategic Partnering to Evaluate Cancer Signatures project, and the Children's Oncology Group (COG), which has an extensive collection of annotated tumor specimens. A subcommittee of the NCI Board of Scientific Advisors (BSA) will provide strong scientific oversight and direction for the initiative. The subcommittee met for the first time at the November BSA meeting, and will meet regularly to provide advice and feedback on the initiative's course.

TARGET will begin with a pilot project that will inform the larger initiative. The pilot—a collaboration involving COG, the University of New Mexico, St. Jude Children's Research Hospital, and NCI—will focus on identifying therapeutic targets for high-risk acute lymphoblastic leukemia (ALL). Already, high-resolution genomic and transcriptomic pro-

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Cancer Research Highlights

Despite Guidelines, PSA Testing Is Common in Elderly Veterans

Many clinicians in the U.S. Department of Veterans Affairs medical system have been ordering prostate-specific antigen (PSA) screening for elderly men. In 2003, 56 percent of nearly 600,000 elderly male veterans had a PSA test performed, even though most guidelines recommend against the blood test for older men who have limited life expectancies because the known harms of prostate-cancer screening outweigh the potential benefits.

PSA screening rates in this population should be much lower than current levels, reported Dr. Louise Walter of the University of California, San Francisco, and her colleagues in the November 15 *Journal of the American Medical Association (JAMA)*. For many men in poor health, screening is more likely to harm them than help them. The study included veterans aged 70 years or older who had no history of prostate cancer, elevated PSA, or prostate cancer symptoms. They were seen at 104 VA facilities.

Men with worsening health were screened at roughly the same rates as men in the best health. Factors such as marital status and region of the country were more important than health in determining screening. The rates for some subgroups of men in the worst health exceeded 60 percent.

An editorial noted that one reason for the high rates is that most men are overly optimistic about their own longevity. Another is that "patients often overestimate both the risk posed by the prostate cancer and the efficacy of treatment," wrote Dr. Peter Albertsen of the University of Connecticut Health Center.

Younger Women Fare Better than Older Women with Ovarian Cancer

Research has shown mixed results when it comes to age and prognosis after ovarian cancer. But a study, appearing early online this month in the *British Journal of Cancer*, lends the statistical strength of NCI's Surveillance, Epidemiology, and End Results (SEER) Program to results showing that younger women have a clear survival advantage compared with older women. Furthermore, younger women who receive uterine-sparing treatment do just as well as women who have standard surgery to treat the disease.

The study includes a nationally representative sample of 28,165 women who were diagnosed with epithelial ovarian cancer between 1988 and 2001. The women were divided according to age groups "very young" (<30 years old), "young" (30 to 60 years old), and "older" (>60 years old), as well as by race, cancer stage, grade, and type of treatment they received—uterine-sparing surgeries versus hysterectomy and/or radical debulking.

The overall 5-year survival for very young, young, and older women was 78.8 percent, 58.8 percent, and 35.3 percent, respectively, with similar trends for early- and late-stage disease. Younger women tended to be diagnosed with early-stage disease more often than older women, and they also received surgery more often, usually a uterine-preserving procedure (71.2 percent versus 14.1 percent and 15.6 percent). Women aged 16 to 40 who had these uterine-sparing procedures had similar survival to women of the same ages who had standard surgery (93.3 percent versus 91.5 percent). "Younger age continues to portend for a better prognosis across ethnic, histologic cell types, and year of diagnosis," the authors wrote, advising that "reproductive-age women who undergo surgical staging should be offered conservative treatment with uterine-sparing surgeries…[and] be treated aggressively."

Adjuvant Radiotherapy Reduces Advanced Prostate Cancer Recurrence

Patients with pathologically advanced prostate cancer who received immediate adjuvant radiotherapy following radical prostatectomy had a significantly reduced risk of PSA relapse, according to a study published in the November 15 *JAMA*.

A total of 425 men were enrolled into the multi-institutional study conducted by the Southwest Oncology Group, and were randomly assigned to either external beam radiotherapy or usual care plus observation. Patients were enrolled between 1988 and 1997, and were followed for a median of 10.6 years.

Although the reduction in the risk of cancer spread to distant sites was not significantly different between the two arms, the study showed that adjuvant radiotherapy significantly lowers the risk of cancer recurrence

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(Highlights continued from page 3)
as indicated by PSA relapse. Median PSA relapse-free survival in the observation group was 3.1 years compared with a median PSA relapse-free survival of 10.3 years in the group receiving adjuvant radiation therapy.

PSA relapse may be an early indication of disease relapse and is associated with considerable patient anxiety. Dr. Bhadrasain Vikram, chief of the Clinical Radiation Oncology Branch in NCI's Division of Cancer Treatment and Diagnosis (DCTD), commented that "If, after the operation, cancer is found to extend beyond the prostate—but not into the lymph nodes—radiation treatment may decrease recurrences. But, radiation also increased the risk of side effects, especially problems with urination."

Future research questions raised by this study include whether radiotherapy is better delivered immediately postoperatively or at time of PSA recurrence which would spare some patients unnecessary treatment, and whether metastatic disease could be significantly affected by identifying and treating subsets of higher risk patients.

Dr. Vikram commented, "In 1988, when this study began, the surgeons' ability to select for operation men with cancer truly confined to the prostate was much less refined. With all the information that is available today prior to surgery, very few men should have cancer found beyond the prostate. For those who do, this study offers valuable information about what to expect, and that should help in deciding the best course of action."

Primary Care Physicians Are Low Prescribers of Tamoxifen

Only a minority of primary care physicians have prescribed tamoxifen for breast cancer prevention since its approval for that use in 1998, and a woman's increased risk of endometrial cancer or blood clots from tamoxifen seems to have less effect on prescribing decisions than other factors, according to a study published online November 13 in the *Archives of Internal Medicine*.

Although tamoxifen has been shown to greatly reduce the incidence of breast cancer among high-risk women, it also has significant adverse effects, including a twofold increase in the risks of venous thromboembolism and endometrial cancer.

In a study of prescribing habits of 350 primary care physicians, University of Pennsylvania researchers found that only 27 percent had prescribed the drug for breast cancer prevention in the past 12 months. The results indicate that prescription of tamoxifen by primary care physicians is strongly associated with logistical factors, such as patient demand and the physician's ability to determine a patient's risk for developing breast cancer. In addition, "physicians with a family member with breast cancer (usually their mother) were more than two times more likely to have prescribed tamoxifen to a patient than physicians without a family member with breast cancer," the researchers reported.

Decisions to prescribe tamoxifen were not correlated with concerns about endometrial cancer or thromboembolism, the scientists found. "Although we did not explore the reasons for this discrepancy, it is possible that it reflects the perception that endometrial cancer is largely a curable disease and that this finding would not be true for other drugs with different adverse effects," they noted.

Combination of Therapies Shows Promise for Cervical Cancer

A new study from the University of Pittsburgh presented at the 2006 American Society for Therapeutic Radiation and Oncology meeting in Philadelphia assessed the addition of both irradiation of the para-aortic lymph nodes (located above the pelvis) and chemotherapy to pelvic radiation therapy for cervical cancer. Because previous trials of this combination have shown excessive toxicity, this study used intensity-modulated radiation therapy (IMRT) to include the para-aortic lymph nodes in the radiation field. IMRT reduces radiation damage to nearby healthy tissue.

Investigators enrolled 36 patients with cervical cancer into the study. In 19 of these patients, cancer had spread to nearby lymph nodes. All patients received pelvic radiation therapy (including brachytherapy in all but two patients), irradiation of the para-aortic lymph nodes, and weekly low-dose chemotherapy with cisplatin.

One patient experienced high-grade gastrointestinal toxicity, and one experienced high-grade genitourinary toxicity. A high-grade decrease in bone marrow activity was seen in 10 patients. All patients completed radiation therapy; only three could not complete the last cycle of chemotherapy.

Thirty-three patients had a complete response to the treatment, though 11 of them eventually developed recurrences during the follow-up period. None of these recurrences were in the para-aortic lymph nodes; most were due to distant metastases.

"These results are promising but inconclusive," stated Dr. Bhadrasain Vikram, from NCI's DCTD. "Further

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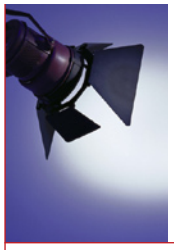

Spotlight

After a Scare, Gleevec Appears Safe for the Heart

In late July, some news organizations reported that 10 patients had experienced heart failure while taking the cancer drug imatinib (Gleevec). That's when Dr. Brian Druker's phone at the Oregon Health & Science University Cancer Institute started ringing.

Dr. Druker led the team that developed imatinib for treating chronic myelogenous leukemia (CML), a potentially fatal disease, in the late 1990s. When the news reports appeared this summer, he was unaware of evidence that imatinib might harm the heart.

But as articles with headlines such as "'Miracle' Cancer Drug May Hurt Heart" began to circulate online, Dr. Druker received hundreds of messages from anxious patients worried about heart failure.

The articles were about a study in the August *Nature Medicine* that referred to 10 patients who developed heart failure while taking imatinib and were treated successfully.

"I was surprised by the study because we hadn't seen any heart failure in patients, and now that we're looking for it, we're still not seeing it," says Dr. Druker, who nonetheless took the concerns seriously and has been monitoring the cardiac health of patients.

His team has not found any abnormalities, and even the hearts of patients who have taken imatinib for 5 or 6 years have appeared normal when tested. In a database of 500 patients, only 1 had died of heart failure.

But back in July, Dr. Druker recalls, "There was a lot of panic." Today, 4 months later, the panic has passed, and some of the concerns about imatinib have been addressed.

The drug's label carries a new precaution, and the drug's maker, Novartis, sent letters to health care professionals about the rare occurrence of severe congestive heart failure, particularly among patients who have risk factors such as diabetes and high blood pressure. CML tends to occur in older patients who have other health conditions.

Also, clinicians are monitoring cardiac health more carefully now and collecting data to study the issue. At present, the available data suggest that the drug, taken by 100,000 patients worldwide for CML and gastrointestinal tumors, is very safe for most patients.

For most patients with CML, a slight risk of heart failure is worth the potential benefit. Without the drug, half of patients with CML would die within 5 years, while 90 percent of patients taking imatinib survive 5 years or more.

The best estimate of the incidence rate is that heart failure occurs in 1 percent of patients. This figure, from a 2003 study in the *New England Journal of Medicine* involving 1,100 patients, had been on imatinib's label.

In the randomized clinical trial, heart failure was less common in the imatinib group than among patients in the control group taking interferon plus cytarabine, which has no links to heart problems (0.7 percent versus 0.9 percent).

"Our review of the data showed how uncommonly cases of heart failure are reported and that in many of the cases, patients had other risk factors that would contribute to heart failure," says Dr. Diane Young, head of Clinical Development at Novartis Oncology.

Novartis and heart failure researchers knew about the cases. They had been reported at a meeting in September 2005 by the authors of the *Nature Medicine* paper, which itself was a follow-up looking at potential mechanisms by which imatinib might affect cardiac cells. The experiments were done primarily in human cells and in mice.

"There was a pretty big overreaction to the paper on the part of the press, and this inflamed the situation," says lead investigator Dr. Thomas Force, clinical director of the Center for Translational Medicine at Jefferson Medical College.

"Our report was simply designed to point out that heart failure can occur and therefore needs to be monitored," he says. "I think the drug will probably turn out to be quite safe if patients are watched."

The findings appeared at a time when many are concerned about the cardiac side effects of some "targeted" cancer therapies.

Drugs such as dasatinib (Sprycel), bevacizumab (Avastin), and sunitinib (Sutent) may slightly increase the risk

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of heart failure. This has led to calls for better monitoring of cardiac function early in clinical trials and beyond (rare side effects often appear after a drug is on the market).

"This study should encourage us to look more carefully for cardiotoxic side effects with these drugs because it does seem to be becoming a larger problem," says Dr. Douglas Mann, chief of cardiology at Baylor College of Medicine at the Texas Heart Institute at St. Luke's Episcopal Hospital.

"We know far less than we need to know about imatinib and cardiac side effects," adds Dr. Mann, who wrote an accompanying commentary in *Nature Medicine*.

He stresses the critical importance of monitoring heart function in patients. Physical examinations may not detect the milder forms of heart failure in patients with no symptoms, yet these patients need to be monitored and, if necessary, treated.

"We need prospective studies," adds Dr. Force. The only reliable way to assess the risk of cardiotoxicity is through studies that test heart function prior to treatment and periodically during the treatment, he says. (Retrospective reviews of clinical trials only detect patients with relatively advanced heart failure.)

But in the meantime, he cautions against scaring patients away from drugs that can help them.

Imatinib has been so effective that some patients were skeptical of the initial news reports. A woman who had just completed a triathlon and another who had been hiking in the San Francisco hills each left Dr. Druker messages, saying "I've never felt better."

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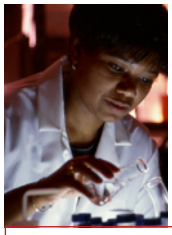

Featured Clinical Trial

Gene Therapy for Metastatic Cancer

Name of the Trial
Phase II Study of Nonmyeloablative Lymphodepleting Chemotherapy Comprising Cyclophosphamide and Fludarabine Phosphate followed by Anti-p53 T-Cell Receptor-Transduced Peripheral Blood Lymphocytes and High-Dose Aldesleukin in Patients with Metastatic Cancer that Overexpresses p53 (NCI-07-C-0003). See the protocol summary at http://cancer.gov/clinicaltrials/NCI-07-C-0003.

Dr. Steven A. Rosenberg

Principal Investigator
Dr. Steven A. Rosenberg, NCI CCR

Why This Trial Is Important
The p53 gene is mutated or deleted (lost) in more than 50 percent of all human cancers. Mutation of this gene often leads to the accumulation of mutant p53 protein inside cells. This abnormal accumulation or "overexpression" of p53 protein occurs because mutant p53 protein is not as easily degraded by cells as normal p53 protein. NCI scientists are now recruiting patients for a clinical trial of a new treatment that targets this common characteristic of cancer cells.

In the trial, researchers will harvest normal T lymphocytes from patients' blood and modify these immune system cells to recognize p53 protein. The modified cells will be enriched in the laboratory and then infused back into the patients. The modified cells will be stimulated further inside the body with interleukin-2 (IL-2 or aldesleukin), an immune system hormone that may also help the cells survive longer.

"We have demonstrated that gene-modified T cells can recognize and kill melanoma cells overexpressing a specific antigen, leading to a clinical response in some patients," said Dr. Rosenberg. "With this trial, we hope to extend this type of immunotherapy to patients with more common cancers."

Patients in this trial will be separated into two treatment groups. Patients with melanoma and renal cell cancer (diseases that respond to IL-2 therapy) will form one group, and those with other types of metastatic cancer will form the other group.

Who Can Join This Trial
Researchers seek to enroll 82 patients aged 18 or over with metastatic cancer that tests positive for p53 overexpression and has progressed despite standard treatment. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/NCI-07-C-0003.

Study Site and Contact Information
This study is taking place at the NIH Clinical Center in Bethesda, Md. For more information, call the NCI Clinical Studies Support Center (CSSC) at 1-888-NCI-1937. The call is toll free and confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.

Notes

Meeting Focuses on Young Adults with Cancer

On November 10–12, several NCI leaders attended a meeting in Austin, Texas, to develop strategies for implementing the recommendations of the Adolescent and Young Adult Oncology (AYAO) Progress Review Group (PRG). The event also served as the inaugural meeting of the Lance Armstrong Foundation's LIVESTRONG Young Adult Alliance, a coalition of organizations committed to improving the survival rates and quality of life for young adults with cancer.

During the meeting, more than 80 representatives from 47 organizations worked together to develop strategies for prioritizing and realizing AYAO PRG recommendations over the next 5 years. The meeting also served as an opportunity for AYA cancer patients and survivors to express their ideas for developing actions to address the disparities experienced by this population.

The Alliance will meet regularly to bring together key voices in the cancer community and work on AYAO PRG recommendations to assist young adults with cancer.

New NCI Web Site Helps Public Analyze Cancer Risks

NCI recently launched an interactive Web site to help people assess and understand their risk of developing cancer. "Cancer Risk: Understanding the Puzzle" at http://understandingrisk.cancer.gov contains explanations of cancer risk, risk factors, and risk exposure—along with information on how to lower risk—for six cancers. The site also contains a section on analyzing news stories about cancer to help people determine the accuracy and applicability of findings reported in the media and on the Web. Links to numerous sources of information, as well as online quizzes to test readers' understanding of cancer risk, also appear on the site.

NCAB to Meet Next Week

The National Cancer Advisory Board (NCAB) will meet November 30–December 1 on the NIH campus in Bethesda, Md., in Building 31, C Wing, Conference Room 10. More information will be posted at http://deainfo.nci.nih.gov/advisory/ncab.htm as it becomes available.

Breast Cancer Research Resource Is Updated

The Breast Cancer Surveillance Consortium (BCSC) has announced an updated Web site at http://breastscreening.cancer.gov, highlighting how to access data and work with BCSC to conduct research on breast cancer screening and biology. BCSC is a group of five research sites linking mammography data with cancer outcomes among women seeking mammograms through community radiology practices. The data set includes more than 5,447,140 mammography examinations and 51,282 women with breast cancer.

Through the Web site, investigators can learn about BCSC investigators, view past publications, access a risk estimation data set containing over two million screening mammograms, and learn how to propose and pursue new studies. ◆

Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih.gov ◆

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files are being obtained on approximately 240 ALL cases. These data will be used to select approximately 200 genes for resequencing, which should occur by mid-2007.

While TARGET is designed to benefit children with cancer, there may also be implications for adult cancer therapeutics development. The relatively simple genomic alterations of most childhood cancers may facilitate therapeutically relevant discoveries that could extend into the adult cancer setting.

With TARGET, we are engaging in a systematic application of state-of-the-art technologies to rapidly identify and validate therapeutic targets in childhood cancers. If successful, it will allow new, more effective treatment approaches to be developed, ensuring that children also will benefit from the ongoing revolution in cancer therapeutics development. ◆

(Highlights continued from page 4)

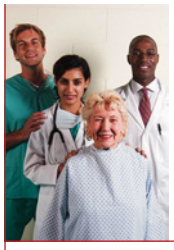
studies need a control group to compare safety with standard radiation therapy. Those must be followed by studies to determine whether the addition of para-aortic irradiation improves survival in comparison to chemotherapy and pelvic irradiation alone." ◆

(Spotlight continued from page 6)

"But people certainly heard the news and were concerned, and I had to spend a lot of time reassuring patients," Dr. Druker says.

He expects that research groups with large numbers of patients will eventually publish data on the incidence of heart failure and imatinib in the scientific literature, and "this will set the record straight." ◆

By Edward R. Winstead



Cancer Center Profile

University of Colorado Cancer Center

Director: Dr. Paul A. Bunn, Jr. • 1665 N. Ursula Street/PO Box 6510, Aurora, CO 80045 • Phone: 800-473-2288 • Web site: http://www.uccc.info

Background

In March 1988, the University of Colorado Cancer Center (UCCC) became the only NCI-designated Cancer Center in the Rocky Mountain region, receiving Comprehensive Cancer Center status in November 1997. In 2000, the outpatient care of UCCC moved from its original campus near downtown Denver to the new University of Colorado at Denver and Health Sciences Center campus (UCDHSC), a "health sciences city" that is being built at the previous Fitzsimons Army base in Aurora, Colorado. A 12-story, 640,600-square-foot cancer research facility opened across the street from the outpatient cancer unit in 2004, helping clinical and basic researchers to collaborate. Recently, UCDHSC formalized a consortium agreement with several partner institutions in Colorado, which both strengthened and broadened the scope of cancer research activities, and extended the benefits of that research to a wider population.

Patient Care

The Developmental Therapeutics/Phase I Program, which started at UCCC 7 years ago and has enrolled more than 600 patients, is one of 16 NCI-funded phase I programs and the only such program in the Rocky Mountain region. The program draws patients from more than nine states. Other features of it include a 3-year Developmental Therapeutics Fellowship Training Program and a translational lab.

The Melanoma Research Clinic at UCCC is one of the largest in the nation, and is staffed by medical oncologists and oncology nurses who specialize in melanoma, dermatologists with particular expertise in pigmented lesions, dermatopathologists, dermatologic surgeons, and surgical oncologists.

UCCC is internationally recognized for work on the prevention, early detection, and treatment of lung and chest cancer, and is a Lung Specialized Program of Research Excellence (SPORE). Within the SPORE are four scientific projects studying the role of altered signal pathways in the pathogenesis and progression of lung cancer, and learning to use these alterations as biomarkers for risk, as well as for developing and evaluating new chemoprevention and treatment strategies.

Research Activities

UCCC is becoming a national leader in structural biology, providing expertise and state-of-the-art nuclear magnetic resonance instrumentation and x-ray crystallography. Recent pioneering studies of chromosomes, chromatin, and gene regulatory complexes represent important strides toward understanding key components of gene expression and cell-growth regulation pathways that may be targeted in future cancer therapies.

Other Notable Programs

UCCC was recently awarded a $3 million grant to provide colon cancer screenings for uninsured legal residents of Colorado to implement and manage the Colorado Colorectal Screening Program. The program began in January 2006 in community clinics in northeastern Colorado, at Denver Health Hospital, and in the city of Pueblo, and has already screened more than 600 patients, found 5 cancers, and prevented an estimated 12 cancers through the removal of large polyps.

UCCC recently became a member of the LIVESTRONG Survivorship Center of Excellence Network. The program provides resources, support, and information to cancer survivors in Colorado and the Rocky Mountain region, and will conduct research to improve follow-up and care of cancer survivors. ◆

The *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads the national effort to eliminate the suffering and death due to cancer. Through basic, clinical, and population-based biomedical research and training, NCI conducts and supports research that will lead to a future in which we can identify the environmental and genetic causes of cancer, prevent cancer before it starts, identify cancers that do develop at the earliest stage, eliminate cancers through innovative treatment interventions, and biologically control those cancers that we cannot eliminate so they become manageable, chronic diseases.

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov. Contact the *NCI Cancer Bulletin* staff at ncicancerbulletin@mail.nih.gov.