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Former Senator Mark O. Hatfield

NIH Dedicates New Clinical Research Center

On September 22, the National Institutes of Health (NIH) celebrated the completion of the new Mark O. Hatfield Clinical Research Center. Government officials, current and former NIH patients and their families, and NIH staff filled the circular Science Court atrium. The patients sat toward the front of the room next to their NIH physicians.

After a welcome by Clinical Center Director Dr. John Gallin, NIH Director Dr. Elias Zerhouni said, "This is a

day of dedication and a new contract with medical research at the beginning of the 21st century." Dr. Zerhouni acknowledged the stakeholders who have made the Clinical Center what it is, including members of Congress who have supported medical research, the NIH staff and construction crew, and the more than 350,000 patients who have participated in clinical trials on the Bethesda campus.

The 870,000 square-foot Hatfield Center connects to the existing Warren Grant Magnuson Clinical Center, which opened in 1953. With the addition of the Hatfield Center, *(continued on page 2)*

Director's Update

Where Cutting-Edge Science Meets Patient Care

With the opening of the new Mark O. Hatfield Clinical Center on the NIH campus, I can't help but think that this next-generation facility will be the site of new research breakthroughs, led in large part by researchers from the NCI Center for Cancer Research (CCR). CCR researchers working in the new clinical center will be at the forefront of the imaging revolution, for example. The recently established Molecular Imaging Program, headed by Dr. Peter Choyke, will be a comprehensive program that spans the discovery-development-delivery continuum. This program's multifaceted

work will include developing imaging probes targeted to specific molecular events or pathways relevant to cancer and the development of novel diagnostic and delivery systems, and then testing these technologies, along with new imaging agents, in early phase trials at the clinical center.

The Hatfield Center also will be the setting of many other initiatives such as the efforts of the Urologic Oncology Branch (UOB), led by Dr. W. Marston Linehan, to attack kidney cancer at the genetic and molecular levels. This work follows more than two decades of discoveries by the *(continued on page 2)*



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(Center Dedication continued from page 1)
the Clinical Center Complex now covers 40 acres and is the largest clinical research center in the world. The center is named in honor of former Senator Mark O. Hatfield (R-Ore.), who served in Congress for 30 years and provided steadfast support for NIH and clinical research.

The Hatfield Center will open with approximately 240 inpatient beds and 80 day-hospital stations. Labs and patient rooms are highly flexible in their design and can be quickly adapted to meet new requirements and changing priorities. Laboratory and office moves are currently underway. Patients will move into the new hospital in December.

Former patient Susan Lowell Butler shared her story at the dedication ceremony. Ms. Butler was diagnosed with simultaneous breast and ovarian cancer 9 years ago, and was treated through a National Cancer Institute (NCI) trial. She recalled when doctors estimated her odds of 2-year survival at less than 20 percent. But Ms. Butler did not give up hope. “I remember how excited I was, calling family and friends and telling them that I’d been accepted into a clinical trial,” she said. “Pretty soon, this place felt just like home.” Ms. Butler also thanked the researchers who worked with her during her treatment and said, “It really is the family of man in all its glory and misery...here in the house of hope.”

Representative C.W. Bill Young (R-Fla.) and Senator Tom Harkin (D-Iowa) introduced Senator Hatfield.

“Only 5 days in my life have been more exciting than today,” Senator Hatfield said, citing the day he got married and the days when his four children were born. He praised the vision, skills, and perseverance of the craftsmen, advocates, scientists, researchers, mentors, staff, patients, and families

who had worked to bring the dream of the clinical research center to reality.

“We are making progress against the top three killers: stroke, heart, and cancer, yet there is more work to be done,” he said. “As my friend Mary Lasker used to say, ‘If you think research is expensive, try disease.’”

The program concluded with the unveiling of a brass plaque and portrait dedicating the center to Senator Hatfield.

HHS Secretary Tommy G. Thompson wrapped up the dedication ceremony by noting that “The Hatfield Center represents an important investment in science and treatment on behalf of the American people. Through its doors will come patients who, in partnership with NIH’s doctors, nurses, and researchers, will try to find answers to some of the most perplexing questions in medicine.” ♦

(Director’s Update continued from page 1)
Branch’s researchers, including the identification of three genes—VHL, Met, and BHD—each related to a different type of kidney cancer. Researchers worldwide have been studying these genetic pathways, especially the VHL pathway, and in partnership with a small pharmaceutical company, UOB researchers have developed new molecular therapeutics that will be tested in early stage trials in the Hatfield Center. Importantly, these trials will incorporate vascular imaging and PET to immediately evaluate patient response to therapy.

The Hatfield Center will also support researchers in NCI’s Division of Cancer Epidemiology and Genetics who have been conducting long-range family studies to identify and track cancers with a hereditary basis. They have also been developing strategic partnerships within the molecular epidemiology community to further accelerate progress in this area.

The NCI trials will benefit from many of the Hatfield Center’s attributes,

including research labs just a few strides from patient beds where tissue samples can be quickly analyzed to assess issues such as biologic responses and molecular changes. Such instant analyses serve to further inform basic science and promote the discovery process while enhancing the real-time clinical decisions—creating the seamless bench-to-bedside-and-back approach that has been a cornerstone of NCI’s intramural research program.

The NIH clinical center has also been an integral part of NCI’s unsurpassed tradition of oncology education and training. Researchers who trained at NCI under world-class scientists such as Drs. Paul Carbone, Emil Frei, Emil Freireich, Vince DeVita, Mark Lippman, Bob Young, and Bruce Chabner have gone on to leadership positions in cancer centers across the country. Fellowship programs in the NCI Surgical Oncology and Dermatology Branches have produced winners of some of the most prestigious national research awards. Translational research courses for postdoctoral and clinical fellows will promote collaboration between basic and clinical scientists, providing instruction in cancer biology and treatment, metastasis, genetics, epidemiology, and identification of molecular targets, among other areas. And, we must never forget that these accomplishments could never have occurred without the selfless dedication of hundreds of nurses, technicians, and staff working as an integrated team.

The opening of the Hatfield Center is an exciting moment in the history of our nation’s biomedical research enterprise. It’s the beginning of a new chapter of NCI’s research success and of hope for a brighter future where suffering and death from cancer is overcome by the steady march of biomedical progress. ♦

*Dr. Andrew C. von Eschenbach
Director, National Cancer Institute*



Spotlight

Advancing Cancer Care at the Clinical Center

The parking garage in the new Mark O. Hatfield Clinical Research Center is a speed bump-free zone—less likely, by that design, to intensify nausea in chemotherapy patients. Down to such details that improve patients' quality of life, the new center is the embodiment of lessons learned from the decades-long union of compassionate patient care and cutting-edge scientific research.

Since its opening more than 50 years ago, the NIH clinical center has played a singular role in advancing cancer care. A mark of this success is the NCI's pioneering work in immunotherapy—boosting the body's own cancer-fighting potential. In the 1980s, NCI Surgery Branch Chief Dr. Steven Rosenberg and his team were largely responsible for advancing the treatment of metastatic melanoma and kidney cancer using the immune system-booster interleukin-2 (IL-2). Known as the grandfather of immunotherapeutics, IL-2 stimulates the continued growth of T cells in the body, generating response rates of 15 to 20 percent for advanced melanoma and kidney cancers. It continues to be part of the standard of care for these cancers.

Today the groundbreaking work in this area continues. Dr. Jeffrey Schlom and his colleagues in the Laboratory of Tumor Immunology and Biology, for instance, have had early success with novel recombinant vaccines to treat gastrointestinal, prostate, and lung cancers. The vaccines equip the immune system to attack tumor cells it would otherwise not recognize as a threat to the body. "This is not only a completely different approach to treating cancer, but one that has the

potential to be virtually free of deadly side effects," Dr. Schlom says.

Meanwhile, Dr. Rosenberg is teaming with others in CCR to convert interleukins and other cytokines with antitumor activity into the tools of another therapeutic line of attack called adoptive immunotherapy. This novel approach uses drugs, gene therapy, and cell transfer to more effectively coax the body's own immune system into action to combat cancer.

NCI research in the clinical center also is focusing on lymphoma—the annual incidence of which has almost doubled over the last 35 years. Dr. Wyndham Wilson and his colleagues in the Experimental Transplantation and Immunology Branch have produced promising results with a five-agent chemotherapy regimen called EPOCH. In early trials, EPOCH yielded a cure rate of 80 percent for the most common adult type of non-Hodgkin's lymphoma, diffuse large B-cell lymphoma (DLBCL). Cure rates with standard therapy are approximately 50 percent.

"These results are based on 12 years of work we have been doing here, building from basic scientific principles," says Dr. Wilson. Because of this success, his team is planning to launch a randomized phase III international clinical trial to compare pharmacodynamic dosing of the EPOCH-regimen agents with standard therapy against DLBCL.

NCI clinical center research is not focused solely on treatment. Researchers from the Division of Epidemiology and Genetics are fueling advances in prevention and early detection through the

Family Studies program—a multidisciplinary research model established 30 years ago, long before the term "team science" entered the medical lexicon. It employs clinicians, epidemiologists, geneticists, and biologists in a collaborative manner, and has set the stage for today's molecular epidemiology research.

Major familial cancer syndromes have been identified through this effort, such as Li-Fraumeni, hereditary breast and ovarian cancer, and hereditary melanoma. Current initiatives for early detection and prevention include a familial melanoma risk-lowering study and trials to test a novel screening tool and risk-reducing surgery to prevent ovarian cancer in high-risk women. "These types of trials are not likely to be funded through a traditional grant mechanism," says Genetic Epidemiology Branch Chief Dr. Peggy Tucker, "and the clinical center forms the infrastructure, onsite collaborative efforts, free evaluation and care, and patient travel activities from which these high-risk, high-impact studies can be run."

Important changes in the delivery of care also have been ushered into practice as a result of NCI work in the clinical center, including the first outpatient clinic for administering chemotherapy, the first outpatient care centers, and the first day hospital—each of which are now standard components at many cancer centers—as well as the first oncology nurses' training program.

For oncology nurses, says Caryn Steakley, CCR deputy clinical director and a registered nurse, the clinical center offers real opportunities to make a difference. "Imagine," she says, "being able to teach patients about research studies and their role as study subjects, participating in developing approaches to symptom management to improve patient outcomes, and connecting with patients and families to improve the health of the nation." ♦

Progress in Cancer Clinical Research



In 1953, the Warren Magnuson Clinical Center opens and its first patient, Charles Meredith, is admitted for treatment of prostate cancer.

Drs. Emil Frei and Emil Freireich achieve the first cures with acute lymphoblastic leukemia (ALL), one of the major malignancies of childhood, with intensive combination therapy.

Most of the 17 Lasker Awards for research on chemotherapeutic treatment of cancer go to researchers who have worked in the Clinical Center. A special award was presented to Dr. C. Gordon Zubrod, NCI's first clinical director.

Dr. Vincent DeVita and his NCI colleagues report the first chemotherapeutic cure of Hodgkin's disease, even in its advanced form.

A special virus-leukemia program is initiated under a special appropriation, included in the FY 1965 appropriation.



X-rays provide critical information in diagnosing cancer.

Using large doses of methotrexate, researchers achieve total cure of choriocarcinoma—a rare cancer of the placenta that was, until then, invariably fatal. It is the first successful treatment for malignancy in a human solid tumor.

Wanda S. Chappell, chief nurse in the blood bank, develops a simple but ingenious method for separating platelets from blood plasma, so that platelets can be used in transfusions for leukemia patients and the rest of the blood can be used by others.

NCI scientists begin to describe families with histories of co-occurring breast and ovarian cancers.

NCI researchers begin to describe cancer clustering in families of children with sarcoma.



NCI conducts chemotherapy testing program, circa 1950.

1950

1960

1970

50 Years of Health and Hope



Most children with ALL can now be treated successfully.

NIH scientists treat first cancer patients with human gene therapy. Two patients receive transfusions of cancer-killing cells removed from their own tumors and armed in the lab with a gene capable of producing a potent antitumor toxin: tumor necrosis factor.

The Children's Inn opens its doors to pediatric patients and their families, thanks to the vision and hard work of NCI's Dr. Phil Pizzo.

NCI researchers demonstrate that adoptively transferred cells can mediate cancer regression in humans, opening the field of adoptive immunotherapy for cancer.



The Mark O. Hatfield Clinical Research Center will provide high-tech, high-touch care to patients.

NCI announces the results of injecting patients in advanced stages of cancer with interleukin-2 or mixtures of this substance with lymphokine killing cells—a 44 percent response rate in 25 patients treated.



Surgery is often an option for cancer treatment.

A second bone marrow transplant unit opens to support NCI protocols.

The FDA approves AZT, initially used for cancer chemotherapy, as the first antiretroviral drug to be used as a treatment for AIDS.

Clinical Center adds new space for NCI and NIAID labs that are focused on AIDS research.

The NCI's pediatric branch hires the Clinical Center's first nurse practitioners.

Identification of p53 as Li-Fraumeni syndrome susceptibility gene.

Groundbreaking ceremonies are held for the Mark O. Hatfield Clinical Research Center.

1980

1990

2000

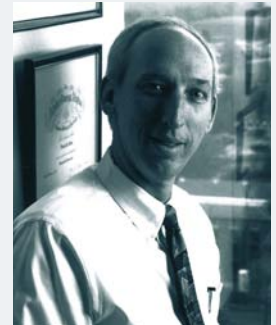
A Conversation with Drs. Frank Balis and J. Carl Barrett

With the opening of the new clinical research center, Center for Cancer Research (CCR) Director Dr. J. Carl Barrett and CCR Clinical Director Dr. Frank Balis shared their thoughts on this new hospital and the role it plays in NCI research.

What are some of the differences between the NIH clinical center and other hospitals?

Dr. Balis: The NIH's clinical center is the world's largest hospital dedicated solely to clinical research, and houses over 50 percent of the NIH-funded general clinical research center beds in our country. Medical care is provided without charge to patients enrolled on clinical research protocols. And the clinical center also provides the unique opportunity to recruit patients from across the U.S. to participate in our trials.

Dr. Barrett: I think another important feature is that the inpatient units in the new clinical center are discipline-based and are shared by multiple NIH institutes that have common clinical research interests, such as bone marrow transplantation. A substantial proportion of the NCI clinical program's research laboratories are located in the same facility and are in close proximity to the patient care units. This design promotes collaboration between NIH institutes, improving the efficiency of the NIH's clinical research efforts and expanding the areas of scientific and clinical expertise involved in the clinical research projects.



Dr. Frank Balis

What are some of the unique aspects of the NCI clinical program?

Dr. Balis: The NCI clinical program is distinct in that it provides close links among the basic, clinical, and epidemiologic scientists in a comprehensive, diverse, and highly interactive environment that promotes exceptional translational research opportunities. NCI's clinical program also routinely makes long-range commitments of resources to support high-risk translational research.



Dr. J. Carl Barrett

Dr. Barrett: Increased collaboration is definitely an advantage offered by the clinical center. The close collaborations among scientists with diverse backgrounds enable the NCI clinical program to fuse new technologies with biology and perform clinical studies that emphasize science-driven, concept-based trials. Since the clinical center draws patients from throughout the country, understudied diseases, cancers with increasing incidence, or cancers involving special populations can be studied here. It also enables us to realize the full spectrum of intervention development from the discovery of agents to their subsequent development into the clinical setting.

Is it fair to say that the clinical program and CCR really play a major role in achieving NCI's mission?

Dr. Balis: Definitely. CCR is widely recognized as a leader in developing novel interventions in the areas of immunotherapy, molecularly targeted therapies for cancers and viruses, and vaccines against cancer and other diseases. And CCR plays a unique role at NCI, enabling us to rapidly focus resources on understudied and rare cancers as well as genetically susceptible populations.

Dr. Barrett: Something that is demonstrated every day in the clinical center is that we continually apply the newest treatment approaches and technologies to clinical research and practice. Our pioneering work in technologies such as imaging and serum proteomics are having a dramatic impact on early diagnosis, treatment, and prevention for cancer patients. And, again, collaboration is a critical part of our work. CCR is actively participating in several trans-NIH initiatives that focus on establishing interdisciplinary and multidisciplinary research teams to advance basic, translational, and clinical research for the most complex and challenging diseases. ♦

Notes from Clinical Center Patients Through the Years

When I was diagnosed with the recurrent cancer, as I recall, it was depression, fear, and the instinct to survive that were with me. When I was accepted into the treatment protocol, hope was awakened in me along with the other emotions. I remember being told that there were about 5 chances in 100 to get a total remission. I was determined then to make it 6 cases in 100... I think it is a miracle that I have been cured of cancer. It is a miracle of hardworking people believing that they can make a difference...that is you and your staff and all the NCI. It is also a miracle of family and friends giving support. Keep up the good work, you really make a difference. Thanks.

— J.H.

I have large B-cell non-Hodgkin's lymphoma with CD-20 and am participating in one of Dr. Wyndham Wilson's clinical trials. I wanted to tell you I have never encountered such a caring, skilled, knowledgeable group of people in my life. The doctors, nurses, and staff all went way beyond anything that was reasonable to detail my treatment, share prepublication copies of research papers, explain to my family what was going on, and generally treat us with kindness and expertise. Granted, I have an aggressive form of cancer, but I still feel like a lucky person to be treated by such high-quality people.

— J.C.

"Hope's a wonderful thing for patients like me, who consider the clinical center to be a place of last resort. When I came here, my doctor had dismissed me; I didn't have anywhere else to turn. I was dreadfully ill and had no idea what I should do. I came here purely for research, but following diagnosis, I was offered treatment. Those of us who have been dismissed elsewhere and have been told there is nothing else to be done...by coming here, we have one more chance to look at our problems, maybe another roll of the dice? another turn at bat, if you will."

— C. W.

"I thank God for this miracle. For the first time in my life I saw doctors who actually listened to me and took the time to answer all my questions—and I had a lot of them [about advanced lymphoma]. I trust the NIH. When other cancer patients ask me about it, whether they have insurance or not, I tell them that they will get the best possible care there."

— D.H.

I think it's good for my daughter. I have pictures of her and all the girls waiting for their CT scans, or in the hospital together getting IL-2 ...everybody's going through the same thing. They all get their blood drawn together. They hold each other's hands. They talk about their medicines and how big the capsules are, boasting, "I can take three (or four) at a time." She doesn't have that anywhere else and I don't either, except at our church. The NIH and the Children's Inn became a second home to us.

— M.D.

We are two sisters who participated in the NCI Hereditary Breast and Ovarian Cancer study. We lost both our maternal grandmother and mother to ovarian cancer. By the time our family was put in touch with NCI in the early 1980s, we were in our 30s and our mother's two sisters had developed ovarian cancer. Our aunts pleaded with us, as they were dying, to do everything that we could to find out why so many women in our family were developing this disease. From the moment we arrived at the NIH center, we were treated not just as case histories, but as an integral part of the research team. Even after our NCI visit, the study team continued their support with follow-up calls to see how we are doing. We both strongly believe that our 20-year experience as NIH research subjects has enabled us to receive the best and most up-to-date medical care.

— N. and J.

Some of these testimonials appear courtesy of Pat McNeese, an NIH clinical center writer.

Guest Commentary by Cokie Roberts

NCI: An Appreciation

Everyone knows that the National Cancer Institute is at the forefront of cancer research, but most people don't know that it's also at the forefront when it comes to caring. For years I have served on the board of the Children's Inn at NIH where terribly sick youngsters and their families can stay while the child is receiving treatment at one of the institutes. I've witnessed the remarkable spirit of the children, many of them bald, talking excitedly about their doctors and nurses.

When my sister Barbara was dying of melanoma, we visited NCI because of the breakthrough work of Dr. Stephen Rosenberg. Little did I know when we made an appointment with this preeminent researcher what a blessing he would become in what little life Barbara had yet to live—and what an important friend he would become to me. From time to time, I called on him about friends, and then I found myself calling him on my own behalf.

After years as a visitor to the NIH campus (I went to school across the street at Stone Ridge and watched the buildings go up) my diagnosis with breast cancer in 2002 suddenly switched my role—now I would be a patient. (We need to come up with another term; those of us with a cancer diagnosis are anything but

patient.) I wanted to be treated at NCI because the smartest doctors in the country work there. I wasn't disappointed on that score, but I also found that I was being treated by doctors and nurses who were kind, considerate, engaged, and blessedly endowed with senses of humor.

Dr. Joanne Zujewski will be my friend for what I hope will be a long and healthy life. She and Dr. Sandra Swain have been unfailingly helpful to me and my family, seeing us through a difficult time, while providing us with the most up-to-date scientific information. They have educated me while treating me.

And I can't say enough about the nursing staff. The respect for nurses at NCI is one of the things that makes it a world-class institution. Knowledgeable and enthusiastic about their work, the nurses know that they have the confidence of the physicians and convey that confidence to their patients. The amount

of clearly presented information they impart about treatments and medications is absolutely invaluable.

While I was still in chemotherapy I took a trip to London to meet my newest grandson. I started running a fever on a Sunday night. I called

the number for Thirteen East, fully expecting to get a recording. Instead, I got Kim who monitored me from afar until she and the doctor she had contacted decided I should go to a hospital. In the few hours I was there, my attending physician talked regularly to the doctor back in



the States until both agreed that I was good to go. Talk about care!

Every day I seem to read some new bulletin about NCI making progress in the battle against this stupid disease. I pray that you may someday put yourselves out of business. Until then, all I can say is please, keep up the wonderful work. And thank you. ♦

Cokie Roberts is a political commentator for ABC News and senior news analyst for National Public Radio.

This *NCI Cancer Bulletin* is produced by the National Cancer Institute (NCI). NCI, which was established in 1937, leads a national effort to eliminate the suffering and death due to cancer. Through basic and clinical biomedical research and training, NCI conducts and supports research that will lead to a future in which we can 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://cancer.gov>.

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