



# CCR...at a glance

A Brief Look at Our Organization and Evolving Culture

*The National Institutes of Health is the steward of medical and behavioral research for the Nation. Its mission is to pursue fundamental knowledge about the nature and behavior of living systems and apply that knowledge to extend healthy life and reduce the burdens of illness and disability.*

*Within this framework, the Center for Cancer Research, part of the National Cancer Institute, conducts distinctive, high-risk, high-impact laboratory, clinical, and translational research in a unique and fostering environment, where it also trains a diverse population of outstanding researchers.*

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## Introduction

The Center for Cancer Research (CCR), an Intramural Research Program at the National Cancer Institute (NCI), has evolved over the past two decades into a premier comprehensive translational research center within the National Institutes of Health (NIH). Our evolution has been patient-focused and persistent.

Seeds of reformation were first planted with the 1994 Marks/Castle Report on “The Intramural Research Program.” This report was released at a time when the intramural research community faced unprecedented opportunities for significant progress yet had little opportunity for budget expansion. The bottom line of this report advised that outstanding science at the NIH should be supported at the expense of less productive programs and efforts. Thus, a strengthened peer review process became a critically important component of ensuring that taxpayers’ dollars supported outstanding projects, and it ensured that progress to improve human health would continue.

A subsequent assessment of intramural research in 1995, the Bishop/Calabresi Report, resulted in decisions that shifted the program’s culture from one with large organizational units assembled around complex research problems to a highly individualized and decentralized scientific workplace. While this reorganization produced much outstanding investigator-initiated research, the new organizational approach failed to maximize the intramural program’s collective scientific wisdom, disciplines, and expertise across the research enterprise.

As knowledge of cancer and HIV/AIDS grew exponentially, it became imperative to establish a culture that could connect our critical pieces of knowledge and leverage our results across the entire research community. Toward that end, NCI leadership created CCR in 2001 with the initial goal of bringing basic and clinical scientists in closer proximity, both physically and organizationally. As CCR has evolved since then, we have added infrastructure to deepen and increase the breadth of our collaborations and partnerships beyond CCR and NIH, and out to academia, foundations, pharmaceutical companies, and industry.

This overview will describe CCR today, including its organization, constant evolution, and distinctive culture. After taking this “glance,” should you want to know more about our research enterprise, I invite you to visit <http://ccr.cancer.gov> for a tour of our labs, accomplishments, and ongoing clinical trials.



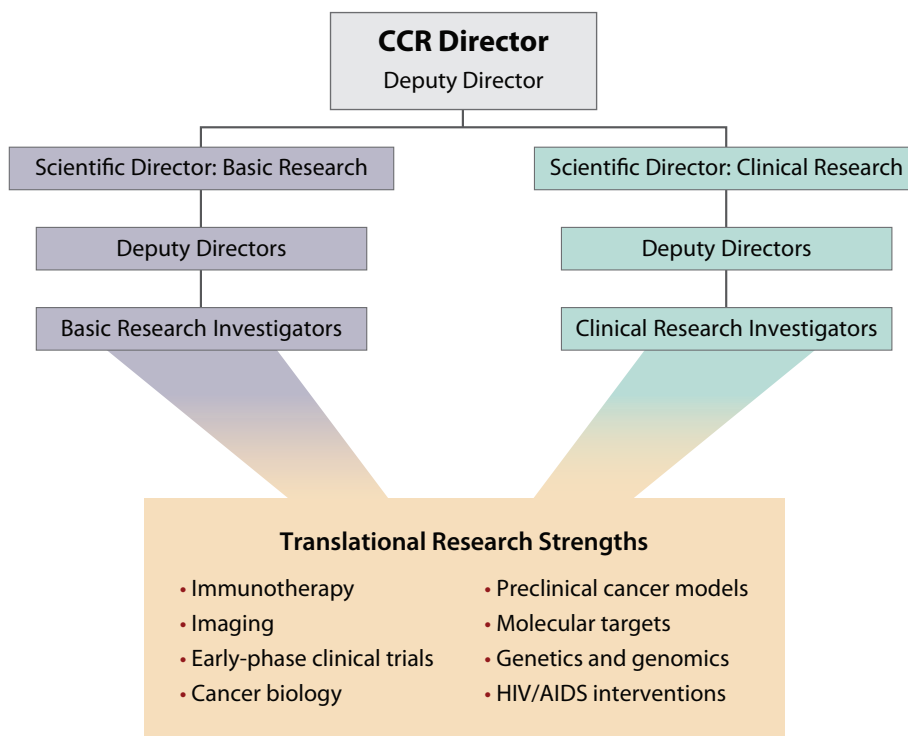
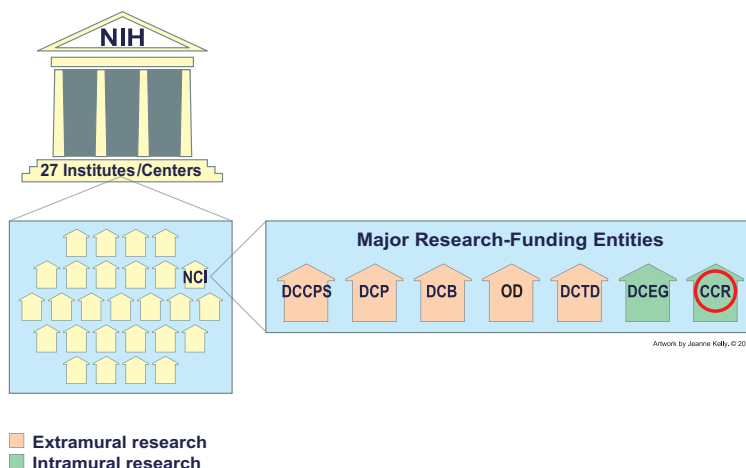
**Dr. Robert H. Wilttrout, Director**  
Center for Cancer Research

# Organization

## Who We Are

### CCR Is an Integral Part of NIH and of NCI

The Center for Cancer Research (CCR) is part of the National Institutes of Health, the Federal Government's primary agency for conducting and supporting biomedical research. Funded within the National Cancer Institute by a Congressional mandate when the National Cancer Act was signed into law in 1971, CCR implements a patient-focused strategic plan to lessen the burden of cancer for all who suffer from this disease. CCR is located on campuses in Bethesda, Gaithersburg, and Frederick, Maryland.



CCR integrates basic and clinical research into translational research strengths that accelerate our progress against cancer and HIV/AIDS. Our on-site intramural cancer research enterprise consists of over 250 principal investigators and nearly 1,000 postdoctoral and clinical fellows who work both individually and in integrated multidisciplinary teams. For a more in-depth view of our community of scientists, please visit: <http://ccr.cancer.gov>.

Center for Cancer Research

## Distinctive Culture

CCR's mission is to inform and empower the entire cancer research community by making breakthrough discoveries in basic and clinical cancer research and by developing them into novel therapeutic interventions for adults and children afflicted with cancer or infected with HIV.

# Distinctive Culture

## CCR's Culture

- Has the critical mass of scientific talent, technology, and long-term support to tackle high-risk, high-impact research
- Moves seamlessly from the lab to the NIH Clinical Center and back to the lab
- Establishes collaborative networks
- Addresses rare cancers and diseases
- Reinvests successes in technology development
- Redeploys resources and responds to:
  - New NCI goals
  - Urgent public need
  - New opportunities

## Tackle High-Risk, High-Impact Research

CCR scientists are encouraged to pursue high-risk research that will have a major impact but may require long-term, sustained support or may be too high-risk for industry or academia to undertake. At present, we are pursuing several high-risk, high-impact research areas that have great potential for accelerating our progress in cancer research:

- Investigating how to capture, share, and use genomics data in diagnosis and prognosis
- Designing and testing new multimodality therapies
- Developing new approaches in immunotherapy and vaccines
- Investigating the use of microRNAs to manipulate cancer gene expression
- Demonstrating the spatial relocation of chromosomes in cancer



## Success after 20 Years!

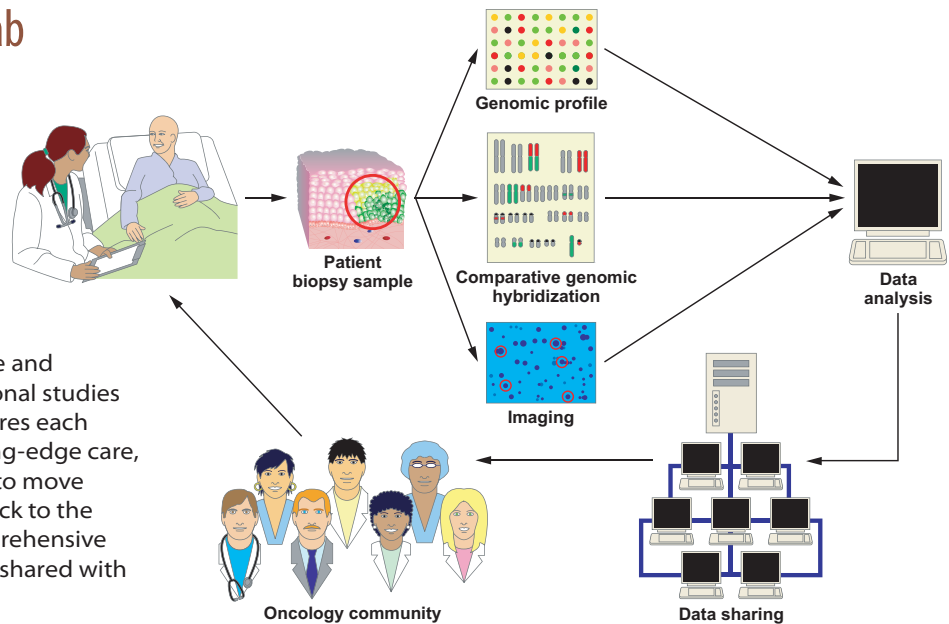
CCR investigators Doug Lowy, M.D. (left), and John Schiller, Ph.D. (right), translated 20 years of research on papilloma viral particles into technology needed for production of a vaccine to prevent cervical cancer.

## Move Seamlessly from Lab to Clinic and Back

### Establish Collaborative Networks

Small numbers of patients make large contribution

CCR's Clinical Program at the NIH Clinical Center is low-volume and patient-centered. Intensive translational studies of specific cancers and diseases assures each patient of careful, customized, cutting-edge care, while permitting research clinicians to move their clinical observations quickly back to the laboratory for refinement. The comprehensive data collected from clinical trials are shared with the oncology community.



## CCR's Collaborative Networks

CCR's research program promotes a collaborative, multidisciplinary environment. Its infrastructure gives CCR the flexibility to leverage strengths of experts from diverse fields. It enables CCR to complement and interface with the activities of the extramural cancer research community, including academia and industry.

- CCR culture supports both investigator-initiated research and team science
- Effective collaborative networks support progress
  - Connect with labs, branches, and NCI leadership
  - Hold small-group principal investigator meetings through Centers of Excellence, Faculties, and Working Groups
  - Lead or join international trials and collaborations
- Broad extramural collaborations accelerate progress



## Empowering Technologies Support High-Impact Research

CCR researchers have access to many core services that can help accelerate their research progress and productivity. In addition, innovative technologies developed at CCR are available to them.

- Molecular Profiling
  - Genomics
  - Metabolomics
- Laser Capture Microdissection (LCM)
- Angiogenesis Program
- Imaging and Microscopy
- Nanotechnology
- Gene Silencing
- Advanced Biomedical Technology
- Animal Models Development
- Bioinformatics, Biostatistics, and Computing
- Molecular Targets Development Program
- Biospecimen Procurement and Processing

# Distinctive Culture

## Treat Rare Cancers and Diseases

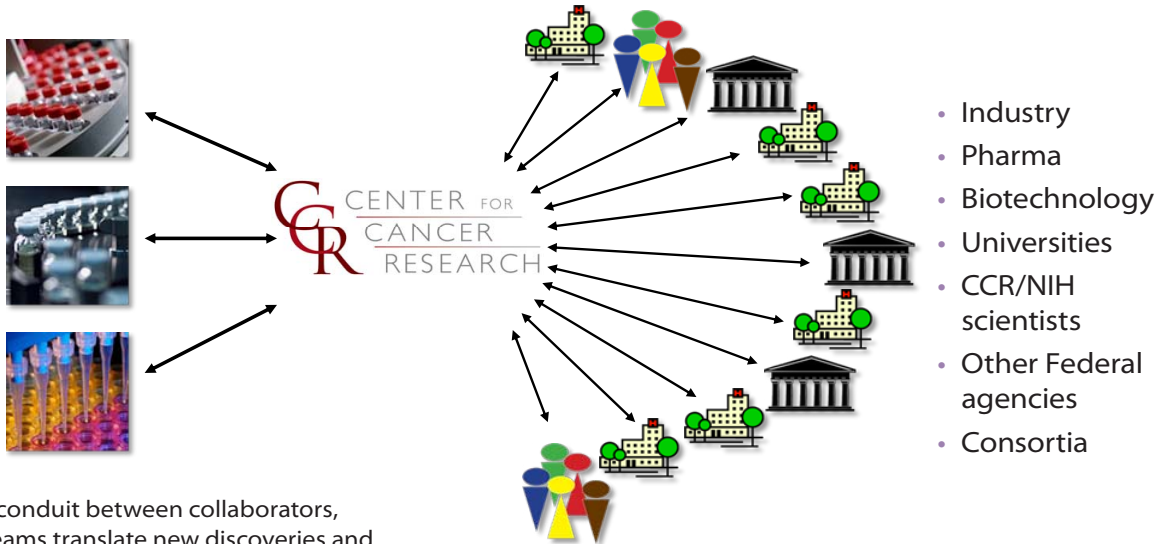


CCR studies rare cancers and diseases that are poorly understood and may not be considered commercially viable for development by Pharma. One example is Xeroderma pigmentosum (XP). Ally suffers from this rare disease, which causes his eyes and skin to be easily damaged by the sun. His caretaker puts salve on his hand, so he can apply it to his lips. CCR research on this disease identified abnormalities in DNA repair genes that have relevance to cancer. Photo credit: Bangor Daily News: Photo by Denise Farwell.

## Some Rare Diseases Treated at CCR

- Xeroderma pigmentosum
- Cutaneous T-cell lymphoma
- AIDS-related primary central nervous system lymphoma
- Gastrointestinal stromal tumor (GIST)
- Mesothelioma
- Thymic carcinoma
- Malignant gliomas
- Neurofibromatosis
- Pancreatic carcinoma

## Establish Partnerships



By serving as a conduit between collaborators, CCR scientific teams translate new discoveries and inventions into effective therapies, approaches, and technologies for detecting, diagnosing, and treating cancer and AIDS patients.



Center for Cancer Research

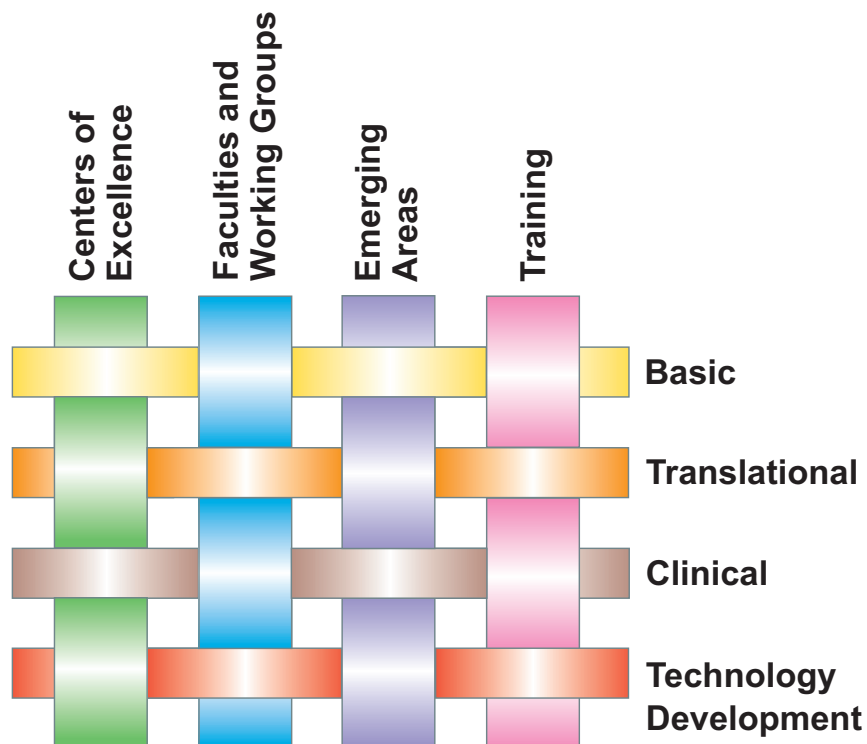
## **Translational Infrastructure**

CCR promotes scientific creativity with its translational infrastructure, an environment in which research teams bring diverse expertise to bear upon the complex problems of cancer and HIV/AIDS.

# Translational Infrastructure

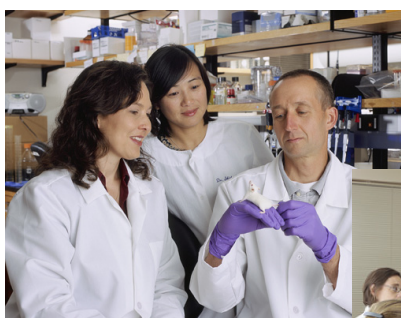
## Translational Infrastructure Is Collaborative

CCR was formed in 2001 to integrate basic and clinical research by encouraging cooperation across the organization to translate discoveries in CCR labs into treatments at the NIH Clinical Research Center. A translational infrastructure makes this possible.



## Translational Teams

CCR's translational infrastructure includes focused Centers of Excellence, Faculties, and Working Groups that leverage the expertise of scientists on-site at CCR and at sister NIH Institutes along with the extramural talent of researchers in academia and industry.



## Collaborative Networks Enable Team Science

### The Centers of Excellence

- Chromosome Biology
- Immunology
- HIV/AIDS and Cancer Virology
- Molecular Oncology
- Integrative Cancer Biology and Genomics

Centers of Excellence lead new initiatives, projects, and collaborations. They position the NCI to play a significant role in interdisciplinary and multidisciplinary translational research and accelerate our progress against cancer and AIDS.

### Faculties and Working Groups

- Discipline-based
- Approach-based
- Disease-based

Faculties and Working Groups foster collaboration, provide awareness of and access to new technologies and clinical resources, and encourage basic scientists to become more knowledgeable and involved in clinical and translational research.

## Center of Excellence Spearheads Trans-NIH Partnership

**IL-15**, a broad stimulant for both innate and adaptive immune response

### CCR researchers:

- Discovered two of the three receptor components for IL-15
- Demonstrated that IL-15 enhances effectiveness of therapeutic cancer vaccines
- Developed new treatments for graft rejection, rheumatoid arthritis, and multiple sclerosis using antibodies to a subunit of the IL-15 receptor

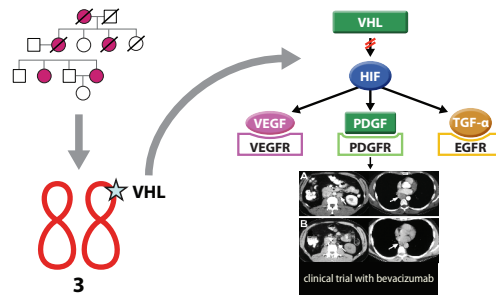
### Partnered with NIAID:

- Initiated GMP (good manufacturing practices) production of IL-15 for both intramural and extramural clinical trials



## Disease-based Faculty Use Multidisciplinary Approach to Cancer

CCR's von Hippel-Lindau (VHL) Research



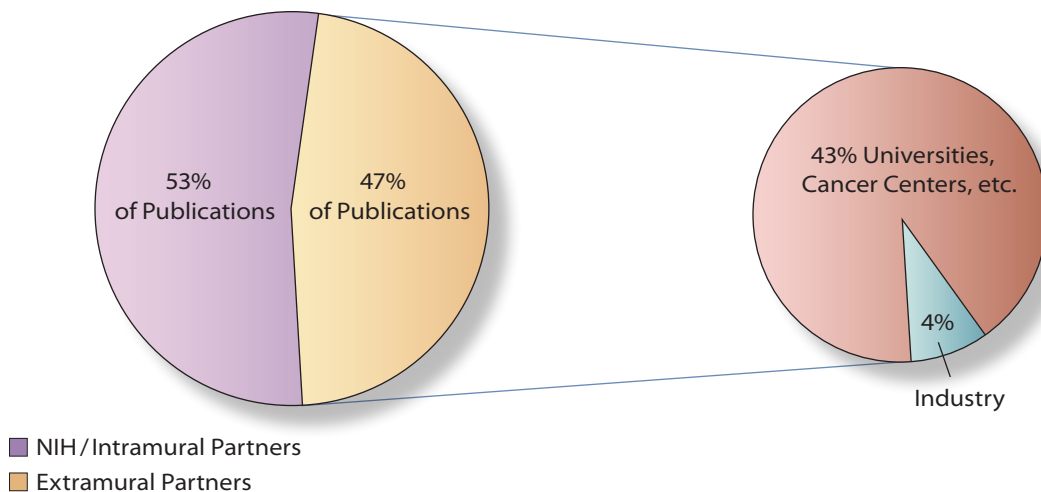
A team of CCR scientists has made significant progress in understanding kidney cancer: from observation in clinic/pedigree, to identification of genes and pathways involved, to DNA diagnostic tests for inherited forms of kidney cancer, to treatment options.

# Translational Infrastructure

## CCR Investigators Publish Collaboratively

47 percent of CCR's published research involves extramural scientists

CCR scientists partner within CCR and NIH as well as with scientists at universities, medical schools, hospitals, government agencies, and other nonprofit and for-profit research facilities in the United States and abroad.



## Rewarding Team Science

CCR review of team science serves as a model

Solving the complexities of cancer requires scientists to move beyond their own disciplines and explore new ways to conduct team science.

Extramural review teams now consider:

- Principal investigator's role and responsibility in multidisciplinary and/or interdisciplinary research
- Leadership role or key contributions to the team
- Quality of overall science
- Degree of contributions
- Originality of contributions
- How the contributions impact the overall project
- Whether a component(s) can be distinctly attributed to the principal investigator

## Serving Others

CCR community-minded researchers:

- Participate in numerous CCR, NCI, and NIH initiatives and projects
- Are members and leaders in scientific associations
- Participate in strategic planning for NIH, NCI, and CCR
- Actively serve on search committees to recruit highly qualified junior faculty
- Support the Children's Inn and NIH activities



Center for Cancer Research

## Clinical Program

The CCR Clinical Program combines insights from preclinical disease models with science-based approaches to human clinical treatment. The collaborative setting allows researchers and clinicians to identify new cancer therapies, both single agents and combinations, and bring them rapidly through early development and clinical testing. When tests are successful, research partnerships with extramural collaborators move new therapies into widespread trials and eventually into clinical practice.

# Clinical Program



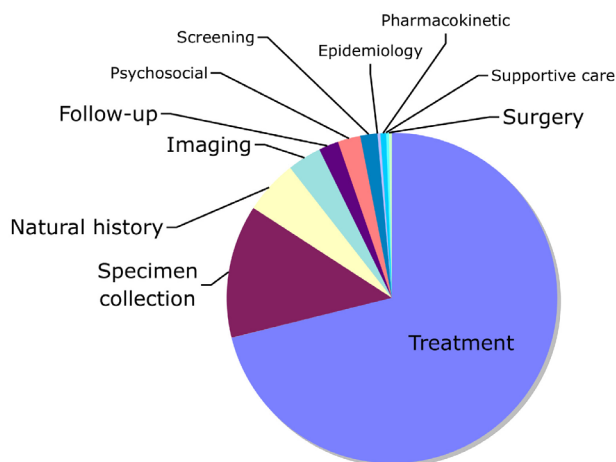
## The NCI Intramural Clinical Research Program

- CCR's intramural clinical research program is far-reaching and active, accounting for 40 percent of the total medical effort at the NIH Clinical Research Center.
- The NIH Clinical Research Center has 242 in-patient beds, 90 day-hospital stations, and multiple outpatient clinics where patients are treated in intramural clinical trials.
- The CCR clinical program treats approximately 4,000 to 5,000 patients per year in 200 studies, enrolling 800 new patients each year.
- Patients are seen in inpatient, outpatient, and day-hospital settings.
- Research activities are multidisciplinary, spanning oncologic diseases from lung, prostate, colon, and breast cancers, as well as lymphoma, to understanding rare cancers and diseases. Research also develops new treatment approaches in transplantation, surgery, radiation, and immunotherapy.

## Distinctive Attributes of CCR's Clinical Research Program

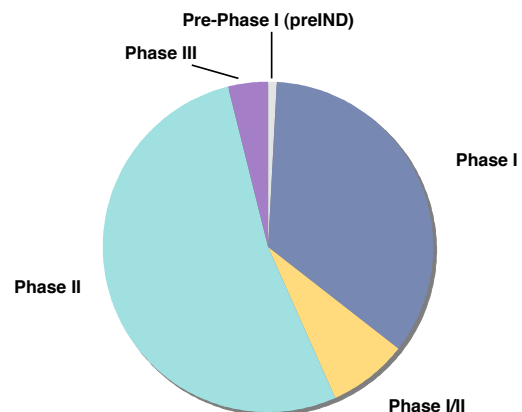
- Integrate basic and clinical research to accelerate translation of advances to benefit patients
- Integrate preclinical cancer models and methods with early clinical development
- Discover and develop molecularly targeted agents and combinations of agents
- Conduct concept-based (science-driven) clinical trials to evaluate new therapies rather than test existing ones
- Develop and deliver novel technologies
- Study rare diseases and underserved cancers
- Provide translational research training

## Types of Clinical Trials



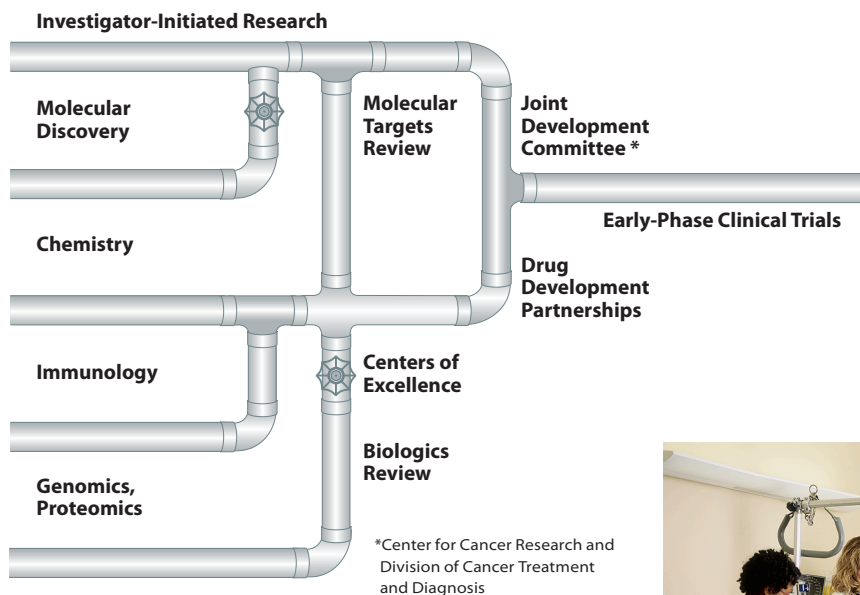
The majority of CCR's trials at the NIH Clinical Center study new treatments.

## Treatment Trials by Phase



The majority of CCR's early-phase studies, from pre-Phase I (preIND) through Phases I and II, are proof-of-principle trials that answer some of the basic questions about optimizing a new drug's dose, safety, and mode of delivery.

## Early-Phase Clinical Trial Pipeline



Many CCR components feed into early-phase clinical trials.

## Clinical Partnerships

CCR's clinical researchers collaborate broadly with many external researchers. Their pooled expertise ensures that innovative findings and technologies are rapidly dispersed throughout the cancer research community.

Examples include:

- **HPV Research, Clinical Trials and Vaccine Development Partnership** is a team of commercial and other government partners who will conduct surveillance in the U.S. post-HPV vaccine licensure.
- **Trans-Institute Angiogenesis Research Program (TARP)** is a multidisciplinary program for collaborative studies in angiogenesis and vasculogenesis. Partnerships include six NIH institutes and the Juvenile Diabetes Research Foundation International (JDRF). TARP and the CCR have partnered to open the Angiogenesis Core Facility, which supports preclinical studies and clinical trials.
- **Hematopoietic Stem Cell Transplantation Partnership** is a "Manhattan Project" approach to overcome the four primary barriers of transplant: graft rejection, graft versus host disease, tumor relapse, and lack of immune reconstitution. Includes extramural Cancer Center with relevant patient population.
- **Lymphoma and Molecular Profiling Project** is an international 10-institution collaboration to establish a molecular classification of human lymphoid malignancies and define molecular correlations of clinical parameters that are useful in prognosis and in the choice of optimal therapy.
- **Glioma Molecular Diagnostics Initiative and REMBRANDT** is a partnership that includes five National Cancer Institute branches, another NIH institute, two consortia, and three SPOREs. All collaborate to accrue 1,000 patients for a national study of gliomas that will correlate extensive prospective clinical data with molecular profiles. The CCR will make the pathological classification of gliomas available as a publicly accessible database with analysis tools.
- **Partnership to Establish Standards for Chronic Graft versus Host Disease (GVHD)** is a collaboration with 100 institutes worldwide to advance the standards of chronic GVHD.
- **Breast Cancer Partnership** is a research program on metastatic breast cancer to the brain that includes a CCR lab working with many extramural labs.
- **Pediatric Oncology Partnerships with Children's Oncology Group and Consortia** is a team effort through which CCR's pediatric oncologists conduct Phase I and II clinical trials at NIH and participate as members of multiple clinical trials consortia, including the COG Phase I/Phase II Developmental Therapeutics Consortium, the Pediatric Brain Tumor Consortium, the Mycoses Study Group, and SARC, the newly formed clinical trials group for sarcomas.



# Clinical Program

- **Cancer Vaccines Partnerships** develop and analyze new recombinant vaccines and vaccine strategies. In addition to the NIH Clinical Center and the National Naval Medical Center, seven cancer centers and the Eastern Cooperative Oncology Group (ECOG) multi-center consortium are conducting collaborative clinical trials for these new vaccines.
- **Therapeutic Immunotoxins Partnerships** test therapeutic immunotoxins developed by CCR at centers nationwide. New antibodies to mesothelin have been humanized, licensed, and are in clinical studies at NIH and at two centers for mesothelioma and pancreatic cancer.
- **HIV and AIDS-Related Agents Partnerships** provided the historical support for research into oncogenic viruses, which led to the co-discovery of HIV as the cause of AIDS and the subsequent development of a diagnostic test in 1984. Many new vaccines and agents are currently being developed in collaboration with industry.
- **Technology and Drug Development Partnerships** enable academia and industry to partner with CCR and produce innovative technology and products such as: laser capture microdissection (LCM) to remove specific cells from microscopic tissue samples; spectral karyotyping to use computer-gathered light waves and assign each chromosome its own distinct hue; PPAR $\alpha$  mouse models to study peroxisome proliferators-induced hepatocarcinogenesis; automated 3-D imaging; and over a dozen FDA-approved new drugs.
- **Comparative Oncology** studies naturally occurring cancer models in animals. Over a dozen veterinary universities have been invited to join the Comparative Oncology Trial Consortium.
- **Local Oncology/Hematology Partnerships** provide patients with easy access to CCR clinical studies. CCR and Associates in Oncology/Hematology (AOH) of Rockville have established a referral system to bring together AOH patients and CCR clinicians.
- **International Partnerships** benefit cancer patients around the world. In a partnership with the King Hussein Cancer Center in Amman, Jordan, CCR will address the prevalence of pediatric cancer in Iraq.
- **National Naval Medical Center Partnership** supports hematology–oncology subspecialty training for clinical fellows, facilitates collaborative clinical research, and improves access to NCI-sponsored clinical research trials for cancer by U.S. Navy and other Department of Defense (DoD)-eligible beneficiaries. Joint protocols developed have benefited the research efforts of both institutions over the years.
- **Gastrointestinal Stromal Tumor Clinic** brings together patients and national experts to evaluate treatment approaches for this rare disease and to develop an effective national clinical trial.

## The Vision for the Future

The CCR is moving toward an era of personalized medicine in which each patient will receive the right therapy at the appropriate dose for the correct duration to best prevent, treat, or manage his or her specific cancer.

### We will reach this era by:

- Blurring the line between imaging and pathology and improving imaging techniques to find lesions at the earliest point possible
- Identifying the molecular pathways and networks through which cancer signals, independent of the tumor's tissue origin
- Disrupting pathways and networks using combinations of therapies to minimize toxicity and maximize therapeutic benefit
- Monitoring the patient with noninvasive imaging for reactivation of the tumor at the molecular level
- Intervening immediately using novel therapies developed and validated through CCR preclinical models followed by design and implementation of early-phase clinical trials





Center for Cancer Research  
**Scientific  
Accomplishments**

CCR researchers lead outstanding investigator-initiated studies and are active in extensive and borderless collaborations. A sustained public investment in these projects enables our scientists and clinicians to collaborate with sister NIH Institutes and with extramural scientists in academia and industry, yielding high-impact milestones in our progress against cancer and HIV/AIDS.

# Tackle High-Risk/High-Impact Research

## Accomplishments

- Contributed key technology for the commercial development of an HPV vaccine to prevent cervical cancer
- Developed novel adoptive cell transfer therapy for metastatic melanoma
- Developed technology to classify lymphoma at molecular level
- Developed BL22 immunotoxin
- Developed monoclonal antibodies to define IL-2 receptor subunits alpha and beta
- Identified genetic mutations linked to hereditary kidney cancer
- Discovered keratinocyte growth factor
- Co-developed, co-discovered, and ran initial clinical trials for first effective AIDS drug
- Developed Spectral Karyotyping (SKY)
- Developed in vivo imaging for ovarian cancer

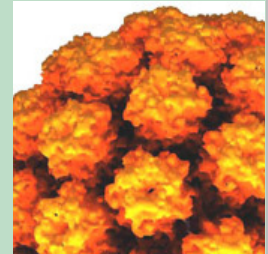
## Making Progress

- Demonstrated proof-of-principle in animals for imaging hypoxia in tumors
- Developed monitoring technology for neurofibromatosis
- Developed automated methods for visualizing cells and viruses
- Showed that replicated adenovirus-based HIV (Ad4-HIV) and SIV vaccines elicit potent protective efficacy
- Identified and clinically evaluated first Hsp90 inhibitors
- Unraveled mechanisms of multi-drug resistance/ABC transporters
- Co-discovered interleukin-15 (IL-15) as part of an immunological synapse between dendritic cells and target NK and CD8 memory T cells
- Identified DNA repair abnormalities in rare disease Xeroderma pigmentosum (XP)
- Discovered better topo I inhibitors
- Developed translational informatics approach to glioma

## Contributed key technology for the commercial development of an HPV vaccine to prevent cervical cancer

**High risk** – Injections of virus-like particles had to trigger a sustained immune response

**High impact** – A commercial HPV vaccine prevents cervical cancer



## Developed novel adoptive cell transfer therapy for metastatic melanoma

**High risk** – Cell transfer therapy had potential for adverse immune cell effects

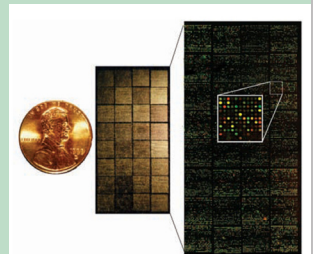
**High impact** – High frequency of response for an otherwise intractable disease



## Developed technology to classify lymphoma at molecular level

**High risk** – Profile must be correct; guides treatment decisions

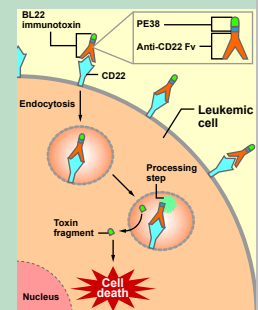
**High impact** – Chip enables accurate molecular diagnosis and informs treatment



## Developed BL22 immunotoxin

**High risk** – Uncharted territory on a rare cancer with a new approach

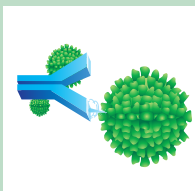
**High impact** – Complete remissions in many patients with drug-resistant hairy cell leukemia



### Developed monoclonal antibodies to define IL-2 receptor subunits alpha and beta

**High risk** – First anti-cytokine receptor monoclonal antibody; first humanized, FDA-approved antibody

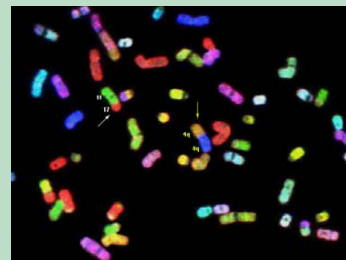
**High impact** – FDA-approved Daclizumab reduces organ-allograft rejection, treats multiple sclerosis, and—armed with Yttrium-90—treats T-cell leukemia/lymphoma and Hodgkin’s lymphoma



### Developed spectral karyotyping (SKY)

**High risk** – Technology for studying cancer chromosomes was not reliable/reproducible

**High impact** – Revolutionized process of karyotyping



### Identified genetic mutations linked to hereditary kidney cancer

**High risk** – Available technology to comb genome was labor intensive

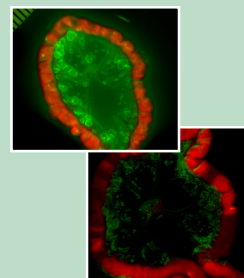
**High impact** – Identifies, screens, and speeds the identification of susceptibility genes; screens families faster; improves therapy design



### Developed in vivo imaging for ovarian cancer

**High risk** – Residual tumor after ovarian cancer surgery could not be imaged

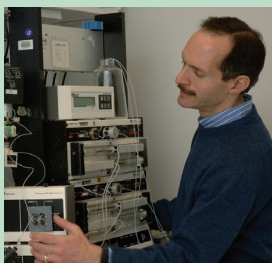
**High impact** –Fluorescent imaging visualizes residual tumor in real time



### Discovered keratinocyte growth factor

**High risk** – Many hurdles; few candidate drugs obtain regulatory approval

**High impact** – FDA-approved Kepivance reduces oral mucositis in patients receiving high-dose chemo/radiation



### Demonstrated proof-of-principle in animals for imaging hypoxia in tumors

**High risk** – Instrument did not exist, needed to create technology from scratch

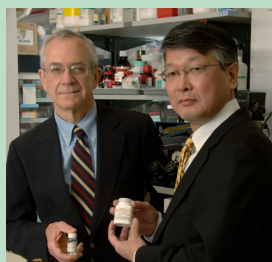
**High impact** – Instrumentation detects hypoxia in vivo; has application to all solid tumors



### Co-developed, co-discovered, and ran initial clinical trials for first effective AIDS drugs

**High risk** – No AIDS drugs had been developed; their clinical benefit was unclear

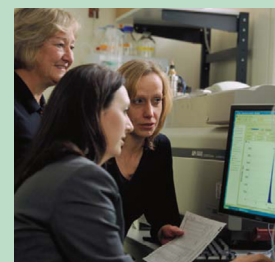
**High impact** – These first AIDS drugs were the foundation for highly active antiretroviral therapy (HAART)



### Developed monitoring technology for neurofibromatosis

**High risk** – No standard treatment available for this rare cancer

**High impact** – Technology to measure neurofibromatosis tumors monitors efficacy of new therapies



# Tackle High-Risk/High-Impact Research

## Developed automated methods for visualizing cells and viruses

### High risk –

Requires visualizing at resolutions 100 times higher than light microscopy

### High impact –

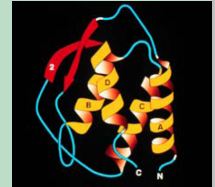
Accelerates understanding of disease mechanisms and vaccine development



## Co-discovered interleukin-15 (IL-15) as part of an immunological synapse between dendritic cells and target NK and CD8 memory T cells

**High risk** – Cytokine was undefined with no prior biological evidence for its existence

**High impact** – IL-15 activates NK and CD8 memory cells; is being produced for clinical use for metastatic malignant melanoma and renal cell cancer and as part of vaccine protocols



## Showed that replicated adenovirus-based HIV (Ad4-HIV) and SIV vaccines elicit potent protective efficacy

**High risk** – HIV vaccine development has eluded scientists for 25 years

**High impact** – Ad4-HIV vaccine is progressing to human clinical trials



## Identified DNA repair abnormalities in rare disease Xeroderma pigmentosum (XP)

**High risk** – Not much known about biology of XP, a rare disease

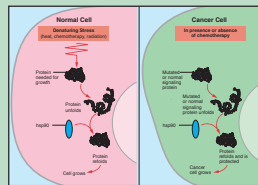
**High impact** – DNA repair abnormalities discovered in XP have relevance to cancer progression



## Identified and clinically evaluated first Hsp90 inhibitors

**High risk** – Had to validate new cancer target and understand mechanisms of activity to optimize drug development

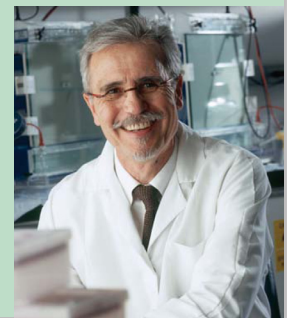
**High impact** – Identification of Hsp90 as a molecular target and development of its inhibitors add to arsenal of anticancer targeted therapies



## Discovered better topo I inhibitors

**High risk** – Needed to reduce toxicity of camptothecin without reducing efficacy

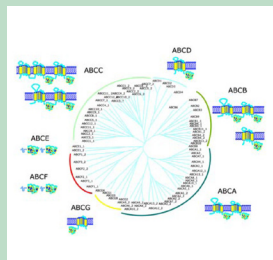
**High impact** – Better drugs that block topoisomerase 1 are moving into clinical trials



## Unraveled mechanisms of multi-drug resistance/ABC transporters

**High risk** – No known explanation for the drug resistance common during cancer treatment

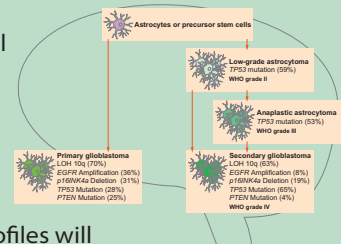
**High impact** – Application of discovery may lead to reversal of resistance



## Developed translational informatics approach to glioma

**High risk** – No successful standard treatment available for this brain cancer

**High impact** – Sharing validated markers of disease and genomic profiles will improve treatment for glioma



Center for Cancer Research

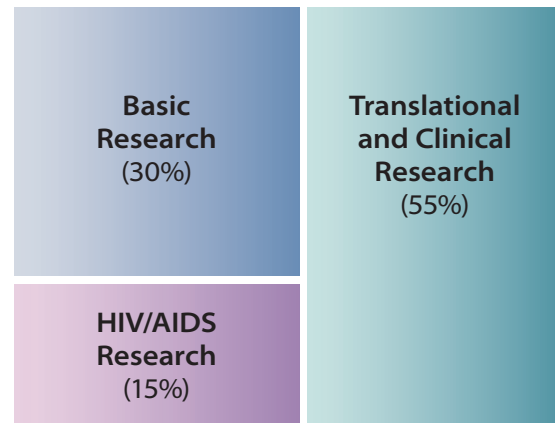
## Planning and Reprogramming

CCR planning and reprogramming is done with a resolute commitment to fund the best collaborative basic, clinical, and translational research, including the study of rare cancers and health disparities, to develop high-impact technology, and to recruit and train a rising generation of new investigators.

# Planning and Reprogramming

## Research Emphasis Today

Fifty-five percent of today's research at CCR is translational and clinical in nature, demonstrating the successful integration of laboratory and clinical research. CCR has cut a large number of underperforming efforts and replaced them with stronger basic science and high-quality translational projects. Additional cuts in unproductive projects will allow CCR to develop areas of high translational priority.



## Rational Approach to Hard Decisions

**Input:**

- NCI Mission and Priorities
- CCR Mission and Priorities
- Reductions in workforce/staff departures
- Programs come to a close
- Board of Scientific Counselors review (rigorous extramural scientific peer review)
- Expert advice

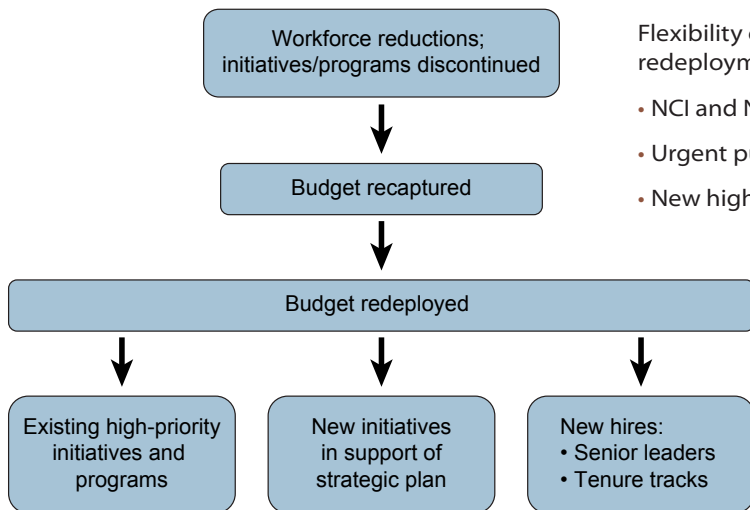
### Input from multiple sources:

- NCI Senior Leadership
- CCR Senior Leadership
- CCR Advisory Board
- Board of Scientific Counselors
- National Cancer Advisory Board



**Output:**

- Reprogram dollars into:
  - New programs/initiatives
  - New tenure-track hires (revitalize CCR)
- PI self-initiated scientific redirection and reprogramming
- High-quality science and outstanding accomplishments
- Implementation of strategic plan



## Flexibility Allows Redeploying

Flexibility of funding approach enables immediate redeployment of resources in support of:

- NCI and NIH mission, goals, and objectives
- Urgent public need (NIH, DHHS)
- New high-priority scientific opportunities

## The Site Visit Process

Assures outstanding research

- Four-year cycle
- Retrospective review
  - Accomplishments
  - Future directions
  - Team science
  - Innovation
  - Mentoring and training
- Site visit team and Board of Scientific Counselors
  - Evaluates the science being performed in light of its cost
  - Encourages high-risk approaches
- Recommendation
  - Team advises CCR Director to continue supporting or to discontinue



## Rewards Team Science

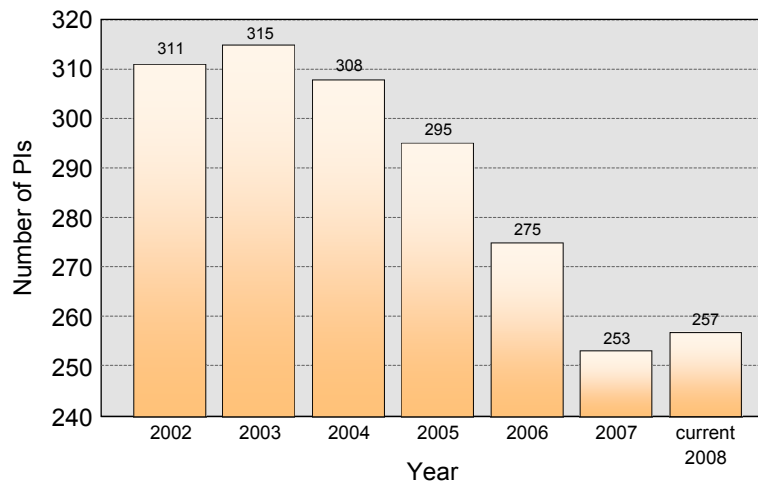
Criteria:

- Principal Investigator's role and responsibility in the multidisciplinary or interdisciplinary research
- Leadership role or key contributions to the team
- Quality of the overall science
- Degree of the contributions
- Originality of the contributions
- How the contributions impact the overall project
- Can a component(s) be distinctly attributed to the Principal Investigator

# Planning and Reprogramming

## Reduction in Number of Principal Investigators (PIs)

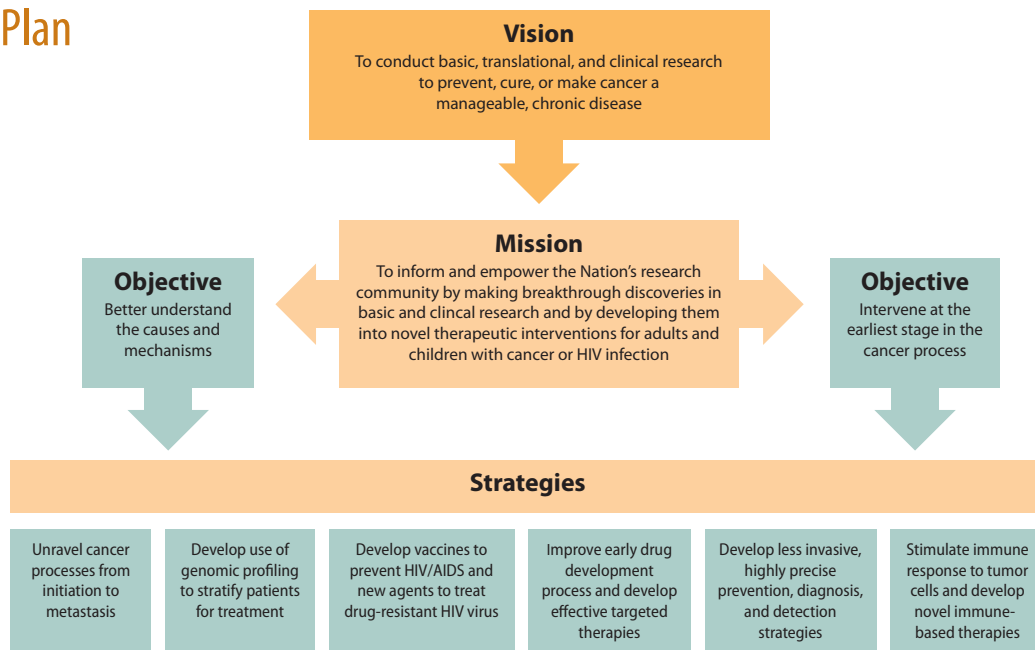
To retain its vitality, CCR, in conjunction with its Board of Scientific Counselors, has taken the difficult steps of eliminating or reducing underperforming programs while creating new programs and initiatives and fully supporting the most meritorious, high-impact research. Overall, the number of Principal Investigators (PIs) has declined by 18 percent from 2002 to 2008, largely because of lab closures and retirements.



## Challenges

- Maintain balance between highly innovative, investigator-initiated research and programmatic efforts
- Support strong basic science that is critical for success of translation to the clinic
- Determine how to do more with less—leverage resources
- Overcome barriers to progress
  - Overly restrictive conflict of interest regulations
  - Technology transfer hurdles
  - Limited flexibility of CCR's Scientific Directors to shift resources
  - Conflict of interest rules restrict membership on Board of Scientific Counselors
  - Increased administrative requirements and restrictions
  - Ineffective centralized infrastructure (Human Resources, Facilities Support, etc.)
  - Coding of money issues inhibit revitalization of physical resources

## Strategic Plan





Center for Cancer Research  
**Technology Transfer  
and Partnerships**

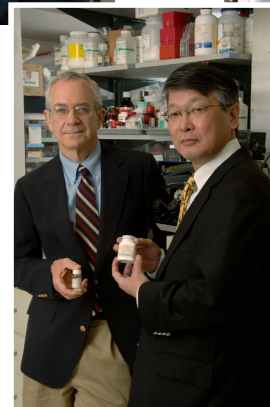
CCR recognizes the importance of building strong scientific partnerships. By partnering with public and private institutions, CCR accelerates the movement of scientific discoveries to the market place for the ultimate benefit of public health.

# Technology Transfer and Partnerships

## Fulfilling Our Mission Through Development Collaborations and New Technologies

### Collaborations

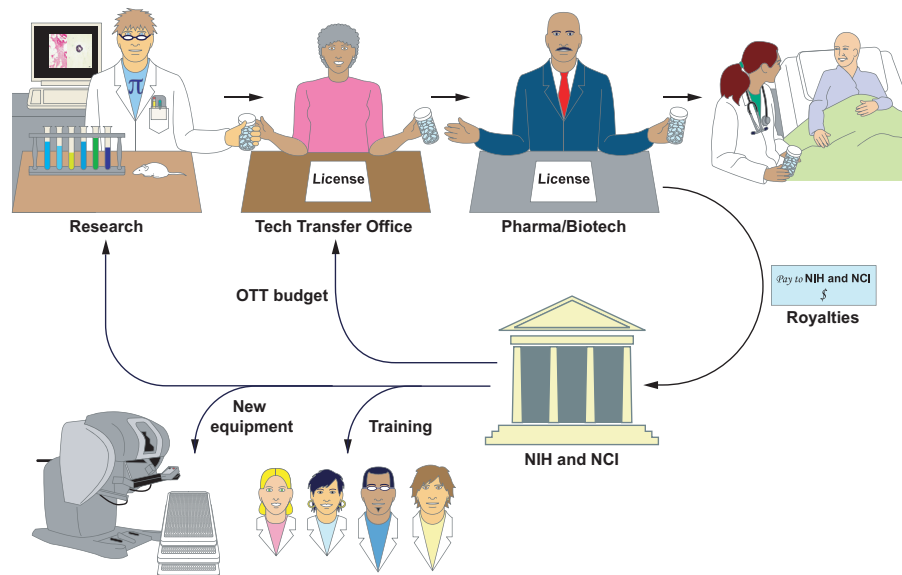
- CCR Lab/Branch
- Trans-NCI
- Trans-NIH
- Intramural/Extramural
- Other Federal Agencies
- National and International Consortia
- Industry
- Pharmaceutical Companies



CCR recognizes the importance of building strong scientific partnerships. Our teams leverage their diverse strengths in various disciplines, approaches, technologies, and knowledge of specific diseases. By partnering with public and private institutions, we accelerate the speed at which we can bring scientific discoveries to the market place for the ultimate benefit of public health.

## Reinvestment of Technology Development Funds tech transfer, training, equipment, and research

CCR establishes CRADAs, patents, and licenses and reinvests the royalties it receives from its inventions to support training, new equipment purchases, and high-impact research.



## Commercial Successes in Fighting Cancer and HIV

### **Gardasil®: A Vaccine against Human Papilloma Virus (HPV)**

- Cervical cancer is linked to HPV infection.
- Clinical trials of Gardasil® demonstrated 100 percent protection against the development of precancerous cervical lesions and nearly complete protection against the development of genital warts.

### **Kepivance®: Improving the Quality of Life for Cancer Patients**

- Mucositis (painful sores and ulcers in the lining of the mouth) affects ~80 percent of patients who undergo chemotherapy and/or radiation treatment prior to bone marrow transplantation, making eating, drinking, swallowing, and talking difficult or impossible.
- Prior to Kepivance®, there was no treatment for this condition.
- Kepivance® benefits ~11,000 adult Americans with hematologic malignancies who undergo bone marrow transplantation each year.

Here are some examples of drugs developed for patients with HIV/AIDS:

### • **Videx/Hivid®: A Reverse Transcriptase Inhibitor**

Treatments that selectively inhibit the replication of HIV by interfering with reverse transcriptase.

### • **Prezista®: A Protease Inhibitor**

A small molecule HIV protease inhibitor used in combination with other antiretroviral agents and in antiretroviral treatment-experienced adult patients, such as those with HIV-1 strains resistant to more than one protease inhibitor.

### • **Vitravene®: An Antisense Drug**

World's first drug developed using antisense technology that offers an alternative for treatment of cytomegalovirus retinitis (CMV-R) in AIDS patients, and delays disease progression.

### **Vaccines and Therapeutics**

- 2-F-AraA – Fludara (1991) Berlex
- Videx® (1991) Berlex
- Hivid® (1992) BMS
- Paclitaxel® (1992) BMS
- Trimetrexate – Neu Trexin (1993) US Bioscience
- Zenapax® (1997) Hoffman La Roche
- Vitravene® (1998) Isis Pharma
- Zevalin® (2002) IDEC Pharma
- Kepivance® (2004) Amgen
- Gardasil® (2006) Merck
- Prezista® (2006) Tibotec Pharma

### **Diagnostics**

- Serological Detection of Antibodies to HIV-1 (1985)
- Serologic Detection of Antibodies to HTLV-1 (1988)
- DNA Probe for Breast Cancer Diagnosis (1998)
- Multi-Replica Blotting Kit for Proteins

### **Instrumentation/Devices**

- Laser Capture Microdissection

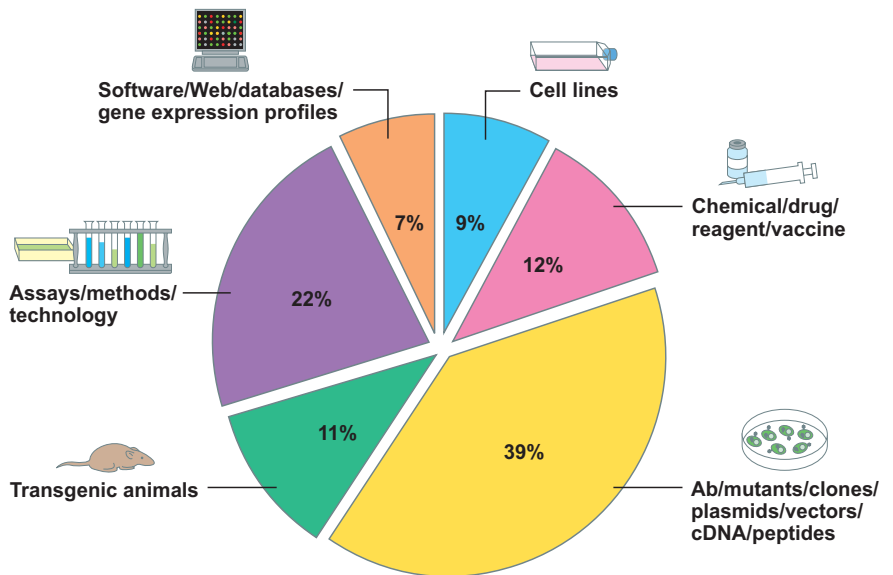


# Technology Transfer and Partnerships

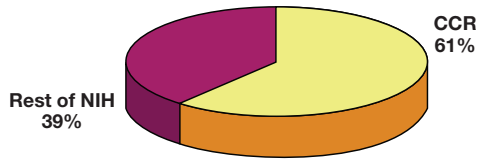
## Research Tools Are Shared

**Research Tools:** The CCR contributed to the extramural research community by sharing nearly 1,000 research materials through material transfer agreements in 2007.

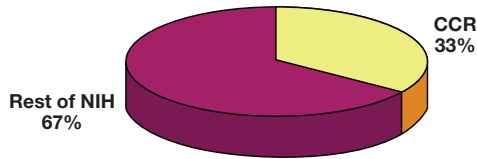
Shared research materials include cell lines, reagents, vaccines, antibodies, plasmids, clones, transgenic animals, assays, and software.



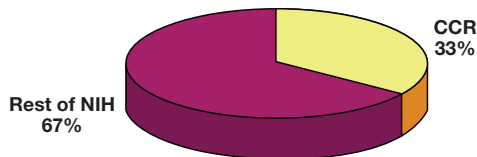
### NIH FY2007 Totals Executed CRADAs



### NIH FY2007 Totals Issued Patents



### NIH FY2007 Totals Executed Licenses



## Excellence in Technology Transfer

When CCR scientists produce research tools, technology, and inventions, in-house legal staff help them file invention reports, license their technology, and establish cooperative research or materials transfer agreements.

This enables innovative intramural researchers to share their intellectual property with the extramural community.

### FY07...by the Numbers

- 125 New EIRs**—Employee Invention Reports (New inventions)
- 39 New Patents**
- 86 New Licenses**
- >1,600 Active Licenses**
- 27 New CRADAs**—Cooperative Research and Development Agreements (formal collaborations with industry)
- 962 New MTAs**—Material Transfer Agreements (exchange of research tools)
- 275 Active Clinical Trials**

Center for Cancer Research

## Training and Mentoring

CCR puts a premium on training the cancer researchers of the future. As part of this mission, numerous programs are offered to students at various levels of training, enabling valuable mentoring to occur. Early career scientists work side-by-side with experienced ones in basic, clinical, and translational laboratories.

# Training and Mentoring

## Training the Next Generation of Scientific Leaders

CCR maintains a robust core of scientists and physician scientists through active recruitment, technology-based training, and exceptional mentorship

### High School

- The Werner H. Kirsten Student Intern Program, NCI-Frederick
  - Exposes high school seniors to research at NCI-Frederick

### High School/College

- Summer Internship Program in Biomedical Research
  - Links undergraduate students to leading scientists in research labs at NIH during the summer
- NIH Undergraduate Scholarship Program
  - Offers competitive scholarships and training to exceptional students from disadvantaged backgrounds
- Cancer Research Interns (CRI) Program
  - Recruits and places students from under-represented or disadvantaged backgrounds into CCR labs
- Biomedical Engineering Summer Internship Program (BESIP)
  - Offers research experience to bioengineering undergraduates who have completed the junior year

### Post Baccalaureate

- Master of Science in Biotechnology with a Concentration in Molecular Targets and Drug Discovery Technologies
  - For graduate students at Johns Hopkins University who gain research experience at CCR
- The Post Baccalaureate Intramural Research Training Award Program
  - For recent college graduates who plan to apply to graduate or professional school
- The Graduate Partnerships Program (GPP)
  - For graduate students enrolled at universities who seek work at the NIH
- Summer Internship Program in Biomedical Research
  - Links graduate students to leading scientists in research labs at NIH during the summer

- NIH Academy
  - For recent college graduates interested in health disparities
- The Technical Intramural Research Training Award Program
  - For college graduates with a bachelor's or master's degree who seek careers as research support professionals
- Year-Off Program for Graduate or Medical Students
  - An interim or year-off research experience
- Biostatistics/Mathematics Training Fellowship
  - Informatics Training Program—currently being developed

### Veterinary School

- Summer Internship Program in Biomedical Research for Veterinary Medical Students
- Comparative Molecular Pathology Research Training Program
  - Offers an opportunity for doctors of veterinary medicine to earn a Ph.D. and gain eligibility for certification as a medical specialist in veterinary pathology. A non-degree postgraduate fellowship training program is also envisioned.

### Medical/Dental School

- Summer Internship Program in Biomedical Research
- Clinical Research Training Program
- Clinical Electives Program for Medical and Dental Students
- Year-Off Program for Graduate or Medical Students
- HHMI-NIH Research Scholars Program



## Postdoctoral Training – Ph.D./DVM

- Cancer Research Training Award (CRTA)
  - For recent doctoral graduates to enhance their research skills at NCI
- Cancer Prevention Fellowship Program (CPFP)
  - For health professionals in multi-biomedical science disciplines to become leaders in the field of cancer prevention and control
- Postdoctoral Visiting Fellowship (VF)
  - For non-U.S. citizens
- NCI Transition Career Development Award (K99/R00) for New Investigators
- Fellowships in Technology Transfer
- NCI/FDA Research and Regulatory Review



## Special Programs/Partnerships

- Johns Hopkins University Partnership in Drug Discovery Technologies
- NCI/GCF (Gynecologic Cancer Foundation) Fellowship
- Interagency Oncology Task Force (IOTF) Research and Regulatory Review Fellowship
- NCI/AFUD Urologic Oncology Ph.D. Postdoctoral Research Training Program
  - This program is designed in collaboration with the American Foundation for Urologic Diseases (AFUD/AUA) to train Ph.D. postdoctoral scientists in the growing field of urologic oncology fellowships

## Postdoctoral Courses/Training

- Translational Research in Clinical Oncology (TRACO)
- Statistical Analysis of Research Data and Statistical Tutorial
- Career Grant Working Group
- Cancer Biotechnology
- Scientific Management Training
- Redox Biology
- Science Writing
- Fellows Editorial Board
  - Free confidential scientific document editing service
- Grand Rounds Seminars

## Postdoctoral Training—M.D. Clinical Investigator Development Program

For board-eligible/board-certified translational researchers to transition from a mentored to an independent investigator researcher, so they will qualify for highly competitive tenure-track appointments in academia, government, or industry.

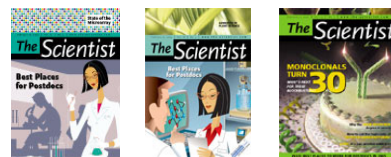
## Clinical Fellowship Program

- ACGME Clinical Residency in Anatomic Pathology
- ACGME Medical Oncology Fellowship
- ACGME Pediatric Hematology/Oncology Fellowship
- Dermatology Fellowship
- Gynecologic Cancer Foundation/NCI Fellowship in Gynecologic Oncology
- Hematopathology Fellowship
- HIV and AIDS Malignancy
- Clinical Training Program
- Radiation Oncology Residency Program
- Surgical Oncology Fellowship Program
- NCI/AFUD Urologic Oncology
- M.D. Research Training Program
- Cytopathology Fellowship Program
- Neuro-Oncology Fellowship Program

## TOP 15!!

“Postdocs hold in high esteem those institutions that do things right: The National Cancer Institute has ranked in the top 15 for all five years.”

***The Scientist, November, 2007***



# Training and Mentoring

## Postdoctoral

- Individual Development Plan
  - Serves as a blueprint to discuss expectations and progress
- Cancer Research Training Award (CRTA) Program Manager oversees CRTA training
- Annual CCR-FYI Colloquium
  - Builds trainees' presentation, organizational, networking, and research skills through poster sessions and oral presentations
- CCR Fellows' seminar series
- Alternative Scientific Careers (sponsored by the NIH Fellows committee)
  - Explores alternative careers in industry, patents/patent law/technology transfer, teaching, science writing/editing, science administration/grants management, science policy
- New Postdoctoral Researchers' Orientation

## Staff Scientist and Staff Clinician

- CCR's investigators are evaluated annually by their lab or branch chief. Mentoring, publication, and career placement of former trainees are discussed at the annual budget meeting and are used to determine any potential increases or decreases in personnel
- Evidence of mentoring activities (publication with their trainees, participation of the trainee at national/international meetings, participation of the trainee in courses and workshops, and positions that are held by their former trainees) is evaluated when investigators go through their quadrennial site visit and BSC review



## Tenure-Track Investigator (TTI)

- Individual career development plan in pursuit of tenure
  - The plan includes seminars, training, meetings with a TTI advisory committee, site visits, and BSC reviews that are scheduled within the Office of Scientific Programs
- Selection of a secondary mentor or an Advisory Committee
- Annual evaluation with his/her Lab Chief and secondary mentor or advisory group
- Meetings with the Scientific Director or his/her designee
- Tenure-Track Investigators Committee
  - To assist the TTI in issues specific to junior principal investigators and pertinent to obtaining tenure at NCI/NIH
- Tenure-Track Retreat


## Senior Investigators

- Sabbaticals
- Centers of Excellence and Faculty Working Groups
  - Further develop leadership and organizational skills through collaborations
- Mentoring training sessions are offered to scientific staff on a regular basis
- Women Scientists' Advisors (WSA) meet with CCR's Director and/or Deputy Director(s) to discuss leadership and other issues pertinent to women scientists, including leadership and mentoring

## Evaluation of Investigator Mentoring

- Annual review of Staff Scientists and Staff Clinicians with their lab or branch chief
- Staff Scientist/Staff Clinician Organization
- Staff Scientist/Staff Clinician Annual Retreat
  - Raises visibility of the scientists, disseminates information for the quadrennial review process, and assists in career development





**Distinctive Alumnae from CCR are contributing as:**

- Department chairs for over 100 U.S. medical centers and universities
- Leaders of many biotechnology companies
- Leaders of many cancer centers
- Scientists in academia and in many government research labs, institutes, and agencies
- Two Nobel laureates
- A Surgeon General



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