CCR is Part of the Intramural Research Program (IRP) of NIH
CCR Is an Integral Part of the NCI

National Cancer Institute

Intramural Divisions
- Division of Cancer Epidemiology and Genetics

Extramural Divisions
- Division of Cancer Treatment and Diagnosis
- Division of Cancer Control and Population Sciences
- Division of Cancer Prevention
- Division of Cancer Biology
- Office of Centers, Training, and Resources
- Center to Reduce Cancer Health Disparities
CCR Overview

CCR Director
Deputy Director

Scientific Director: Basic Research
Deputy Directors
Basic Research Investigators

Scientific Director: Clinical Research
Clinical Director
Deputy Directors
Clinical Research Investigators

Translational Research Strengths
- Immunotherapy
- Imaging
- Early-phase clinical trials
- Preclinical cancer models
- Molecular targets
- Cancer genetics
- HIV/AIDS therapy
Center for Cancer Research: Organization

CCR

Clinical Branches

- Dermatology
- Experimental Immunology
- Exper. Transplantation & Immunology
- Genetics
- HIV and AIDS Malignancy
- Medical Oncology
- Metabolism
- Neuro-Oncology

Basic Laboratories

- Pediatric Oncology
- Radiation Biology
- Radiation Oncology
- Surgery
- Urologic Oncology
- Vaccine*
- Molecular Imaging
- Pathology

* Also has basic component
Center for Cancer Research: Organization

Basic Laboratories

- Basic Research
- Cancer and Developmental Biology
- Chemical Biology
- Gene Regulation and Chromosome Biology
- Biochemistry and Molecular Biology
- Cancer Biology and Genetics
- Cancer Prevention
- Cell and Developmental Signaling
- Cell Biology
- Cellular and Molecular Biology
- Cellular Oncology
- Comparative Carcinogenesis
- Experimental Carcinogenesis
- Experimental Immunology
- Genomic Diversity
- Human Carcinogenesis
- Immune Cell Biology

- Metabolism
- Molecular Biology*
- Molecular Immunoregulation
- Molecular Pharmacology
- Population Genetics
- Protein Dynamics & Signaling
- Receptor Biology and Gene Expression
- Tumor Immunology and Biology
- Macromolecular Crystallography Laboratory
- Mammary Biology and Tumorigenesis
- Molecular Targets
- HIV Drug Resistance Program*
- Structural Biophysics
- Cell and Cancer Biology
- AIDS and Cancer Virus Program (SAIC)
- CCR Nanobiology
- Mouse Cancer Genetics

* Also has clinical component
Laboratory of Cancer Biology & Genetics

- Conducts an integrated research program designed to elucidate the cellular and tissue changes associated with specific stages of carcinogenesis, to detect genetic modifiers fundamental to cancer susceptibility and progression, to define the molecular mechanisms involved in the pathogenesis of major human cancers, and to develop rational approaches for cancer prevention and treatment.
Merlino Lab: Melanoma Mouse Models

Environmental Agent
Neonatal UV Radiation

Genetic Engineering
Deregulated Signaling of the MET Kinase

Melanoma histopathology

Cutaneous Malignant Melanoma in the Mouse

Human
Mouse

GFP-Labeled Melanoma
CCR Vision

To integrate basic, translational, and clinical research to make cancer preventable, curable, or chronically manageable
CCR Mission: Focus on the Patient

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 Attributes of CCR’s Clinical Research Program

- Integrate basic and clinical research to accelerate translation of advances to benefit patients
- Integrate genetically engineered mouse models and methods with early drug 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
- Integrate personalized medicine into all clinical trials
Seamless Movement from Lab to Clinic to Lab

- Patient biopsy sample
- Genomic profile
- Sequencing
- Imaging
- Data analysis

Oncology community

Data sharing
CCR Seeks to Achieve its Mission by:

• Performing rigorous basic scientific research

• Translating these advances rapidly from the laboratory to the clinic

• Developing innovative technologies for detection, diagnoses, and treatment

• Pioneering novel interventions for underserved patient populations and rare cancers

• Sharing expertise, scientific data and technologies

• Training future physician-scientists and biomedical researchers
Cross-Cutting Initiatives Promote Programmatic Integration
Research Emphasis Today

- Basic Research (30%)
- HIV/AIDS Research (15%)
- Translational/ Clinical Research (55%)
CCR Labs and Branches Are Woven Together Around Strategic Priorities

• Understand the Cancer Process from Initiation to Metastasis

• Interrogate the Molecular Genetics of Cancer

• Improve Cancer Prevention, Early Detection, and Diagnostic Approaches

• Develop and Validate Novel Molecularly Targeted Interventions

• Harness the Immune System to Combat Cancer

• Discover and Develop Approaches to Combat HIV/AIDS and AIDS-associated Malignancies
The Centers of Excellence serve to support the IRP’s dedication to long-term, high-risk, innovative basic and clinical research.

- Immunology - Robert Wiltrout, Head
- Chromosome Biology – Gordon Hager, Head
- HIV and Cancer Virology - Stuart LeGrice, Head
- Integrated Cancer Biology and Genomics - Snorri Thorgeirsson, Head
- Genitourinary Malignancies- Marston Linehan & William Dahut, Co-Heads
Collaborations and Partnerships

CCR recognizes the importance of building strong scientific collaborations and partnerships. Our team science approach leverages our diverse strengths in various disciplines, approaches, technologies, and knowledge of specific diseases. By partnering with others, we accelerate the speed at which we can bring scientific discoveries to the marketplace for the ultimate benefit of public health.
Clinical trials performed using an exploratory Investigational New Drug (IND) facilitate targeted therapies entering early phase evaluation where the target can be carefully monitored. The goal of this new guidance is to safely shorten the timeline for drug development. As part of the DCTD-CCR collaboration, novel agents for high-priority targets originating from extramural researchers will be eligible to take advantage of intramural resources.
Commercial Successes in Fighting Cancer and HIV

Vaccines and Therapeutics

- 2-F-Ara-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
- Prezista® (2006) Tibotec Pharma
- Cervarix® (2009) GSK

Diagnostics

- Serological Detection of Antibodies to HIV-1 (1985)
- Serological 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
CCR Accomplishments

Accomplishments

• HPV vaccines to prevent cervical cancer
• Novel immunotherapies for melanoma
• Antibodies and immunotoxins for rare cancers
• Developed technology to classify lymphoma at molecular level
• Identified genetic mutations linked to hereditary kidney cancers
• Discovered keratinocyte growth factor
• Developed several drugs that contributed to HAART therapy
• Developed spectral karyotyping (SKY)
• Developed in vivo imaging for ovarian cancer

Making Progress

• Demonstrated proof of principle in animals that image hypoxia in tumors
• Developed monitoring technology for neurofibromatosis
• Developed software to automate 3D visualization of cellular structures
• Developed adenovirus-based HIV vaccine that gives best protection to date
• Brought Hsp90 inhibitors to clinical trials
• Unraveled mechanisms of multidrug resistance/ABC transporters
• Co-discovered and unraveled cytokine IL-15
• Identified DNA repair abnormalities in Xeroderma pigmentosum
• Discovered better topo I inhibitors
• Developed translations informatics approach to glioma
Virtually all cases of cervical cancer are linked to HPV infection

- In U.S.
  - 9,700 new cases of cervical cancer/year
  - 3,700 deaths attributed to HPV/year

- Worldwide
  - cervical cancer is the 2nd most common cancer in women
  - over 470,000 new cases/year
  - over 233,000 deaths/year

- Clinical trials of Gardasil® demonstrated 100% protection against the development of precancerous cervical lesions and nearly complete protection against the development of genital warts.
- In poorly-resourced regions of the world, HPV immunization may prevent several hundred thousand cancers annually, many of which affect relatively young women.

Douglas Lowy and John Schiller

Source: NIH OTT & NCI TTB
Divide and Conquer Complex Cancers

Dissecting Cancer into Molecularly and Clinically Distinct Subgroups by Gene Expression Profiling

Diffuse Large B Cell Lymphoma

Activated B Cell-like DLBCL (ABC)  Germinal Center B Cell-like DLBCL (GCB)  Primary Mediastinal B Cell Lymphoma

Genes

Lymphoma Biopsies

High
Low
Gene Expression

Louis Staudt
Empowering Technologies Support High-Impact Research

Access to many programs and core services to accelerate research progress and productivity

- Animal resources and services
- Bioinformatics and Biostatistics
- Clinical Research
- Flow Cytometry
- Genetics and Genomics
- Imaging and Microscopy
- Microarrays
- Nanotechnology
- Pharmacology
- Proteins and Proteomics
- Publications and Graphics
- Repositories
- Structural Biology
- Virology Research
CCR Training

CCR offers training to young scientist at several levels of education:

Training programs exist for:

- High School students
- College students
- Post Baccalaureate students
- Veterinary School students
- Medical and Dental School students
- Post Doctoral Training -- Ph.D. / D.V.M.
- Post Doctoral Training -- M.D.
- Clinical Fellowship Program

Professor, Scientist, Clinician, Tech, Admin, etc.
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
- Comparative Biomedical Scientist Training Program for veterinarians leading to a Ph.D.
Comparative Biomedical Scientist Training Program
Trainees are graduate veterinarians with the D.V.M. degree leading to a Ph.D. and specialty board certification

- Veterinary pathology
- Molecular pathology
- Human pathology comparisons
- Medical research
- Animal models of human disease
- Form interdisciplinary teams

Mark Simpson
While most of our alumni remain in the US (61%), many are conducting research abroad, including:

- Canada
- Mexico
- Chile
- Columbia
- Argentina
- Brazil
- Australia
- New Zealand
- Singapore
- Thailand
- Japan
- Korea
- China
- India
- Turkey
- Israel
- Egypt
- Cameroon
- South Africa
- Russia
- Slovenia
- Ukraine
- Bulgaria
- Greece
- Germany
- Czech Republic
- Hungary
- Austria
- Poland
- Italy
- France
- Spain
- Switzerland
- Belgium
- Netherlands
- UK
- Ireland
- Sweden
- Norway
- Denmark
- Finland
- Iceland
Distinctive Alumni

CCR is consistently rated among the top institutions in which to train*

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

*The Scientist: Best Places for Postdocs
Quality Mentors

Nationally Recognized CCR Investigators

**National Academy of Science**
S. Adhya, S. Gottesman, D. Lowy, I. Pastan, M. Potter*, M. Singer*, T. Waldmann, S. Wickner, C. Wu

**Institute of Medicine**
M. Gottesman, R. Hodes, E. Jaffe, S. Katz, C. Klee*, M. Linehan, D. Lowy, I. Pastan, S. Rosenberg, T. Waldmann, C. Wu

**American Academy of Arts and Sciences**
S. Adhya, M. Gottesman, S. Gottesman, C. Klee*, S. O’Brien, I. Pastan, M. Singer*
T. Waldmann, S. Wickner, C. Wu
Vision for the Future

- Focus on testing new science-based hypotheses interrogating a disease or disease process
- Maximize our understanding of how to intervene in the disease process by interrogating the cancer network using genetic, proteomic and imaging tools
For More Information

On the CCR visit:
http://ccr.nci.nih.gov/

For training opportunities visit:
http://www.training.nih.gov/postdoctoral/