



Strategic Initiative: Reengineering the Intramural Research Program

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&
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NCI Strategic Initiatives

Strategic Initiative	Champion
Bioinformatics	Ken Buetow
Integrated Clinical Trials System	Jim Doroshow Howard Fine
Strategic Development of Cancer Interventions	Ann Barker
Overcoming Health Disparities	Harold Freeman
Early Detection, Prevention, Prediction	Bob Croyle
Determination of Risk Factors	Joe Fraumeni
Integrated Cancer Biology/ Fostering Interdisciplinary Science	Dinah Singer
Re-Engineering the Intramural Program	Joe Fraumeni

Reengineering the Intramural Research Program ...

- Is not a Reorganization
- Independent investigator-initiated research will continue as the primary emphasis
- The Intramural Research Program will support and encourage translational research projects, initiatives, and programs
- Recognizes the existing strengths and builds upon them through Faculties, Working Groups, Initiatives, and Partnerships

The Intramural Research Program: DCEG

- The Division of Cancer Epidemiology and Genetics (DCEG) has as its focus population-based research on environmental and genetic determinants of cancer and a long tradition of leadership in cancer epidemiology.

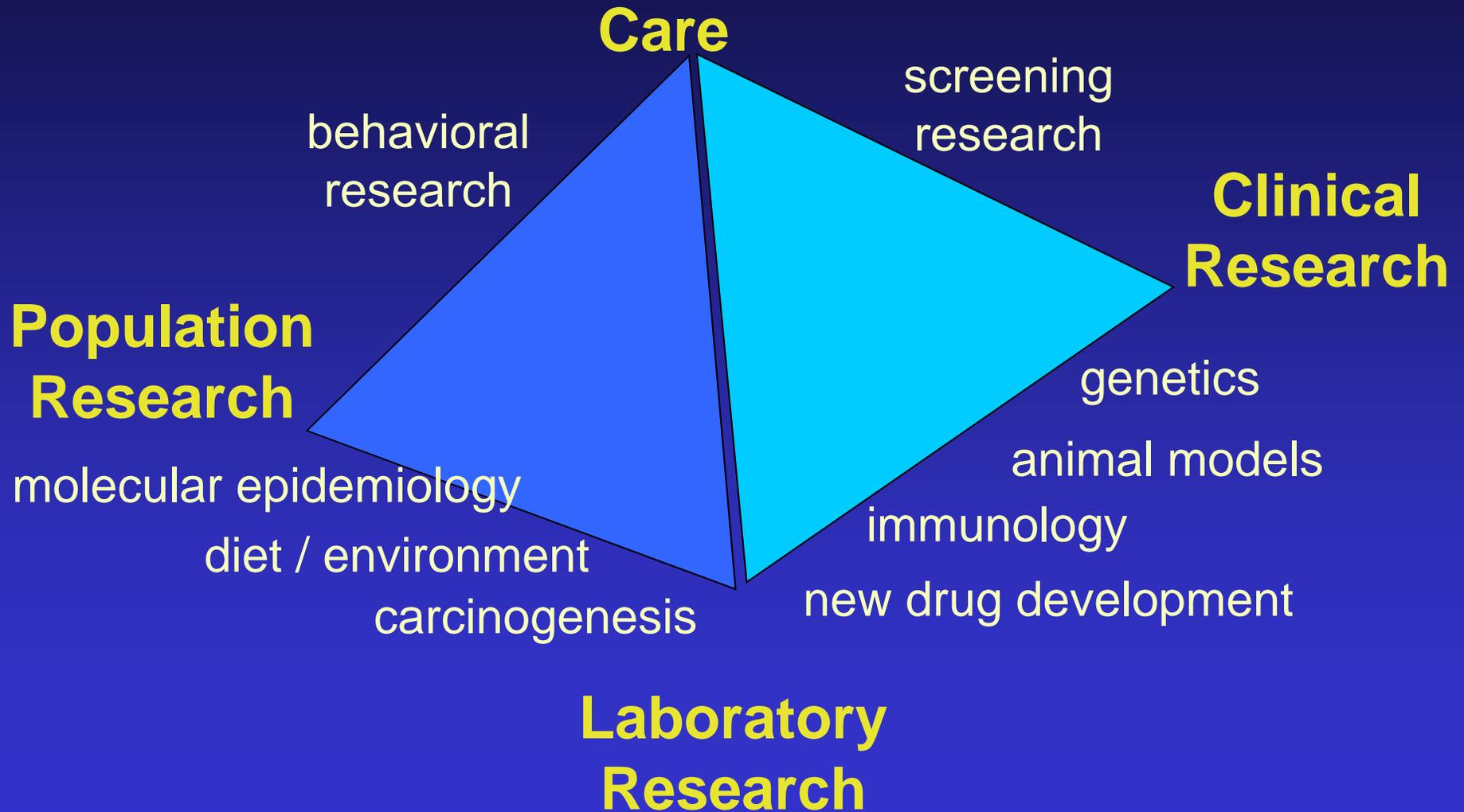
The Intramural Research Program: CCR

- The IRP was reorganized in 2001 to create the Center for Cancer Research.
- CCR Mission: To reduce the burden of cancer through exploration, scientific discovery, and translation of basic research to cancer prevention, diagnosis, and treatment.

Together, DCEG and CCR are well positioned to create a premier center of cancer research.

- A strong basic science foundation coupled closely with innovative technology development and outstanding clinical investigators within the NIH Clinical Center, and population scientists afford the IRP a unique opportunity to achieve this goal and to provide outstanding training in basic, clinical, epidemiologic, and translational research.

How Translational Research Should Work



Adapted from Karen Antman

Opportunities for the IRP

- The opening of the NIH Clinical Research Center in 2004
- The establishment of new consortia with extramural investigators and the IRP
- The development of new technologies in the IRP
- The need to foster new approaches to science (NIH Roadmap)

Unique Qualities of the IRP

- Close link between basic, clinical, and population research in a comprehensive and interactive environment
- Long-range commitment of resources
- The ability to fuse new technologies and biology
- An ability and commitment to respond quickly to urgent public health needs identified by the Institute, NIH, DHHS, and Congress
- A centralized and collaborative program of epidemiologic research that has access to relevant populations and is poised to investigate “natural experiments” whenever and wherever they occur
- Access to the NIH Clinical Center, which contains more than 50% of the NIH-funded general clinical research center beds in the U.S.

Unique Qualities of the IRP (cont)

- An emphasis on discovery of agents and origination of clinical studies rather than simply evaluating effects of known drugs
- Availability of medical care that is provided without charge to patients enrolled on NCI protocols, including coverage of patients' travel, and for children and minors participating in intramural studies, travel for parent or guardian
- The opportunity to recruit patients from across the U.S. making possible clinical studies that emphasize science-driven (concept-based) trials and allowing particular focus on understudied diseases, cancers with increasing incidence, or cancers involving special populations
- An environment conducive to the recruitment, training, and retention of fellows in transdisciplinary research.

Reengineering Process

- “All-PI” meetings were held in Frederick and Bethesda to introduce the Strategic Initiative
- Feedback obtained from the PIs through a web-based system
- Focus groups held on each goal to solicit input from the IRP, other NCI Divisions and Division Directors
- Guidance and input received from the BSC in July and November
- Solicit input in writing and through meetings with NCAB and other extramural experts (SPORE meeting)

Objectives for IRP Reengineering

1. *Define and enhance the value added of the Intramural Research Program*
2. *Develop innovative new technologies and approaches for cancer discovery, prevention, detection, diagnosis, and treatment*
3. *Facilitate the development of a unique clinical research program in the IRP for delivery of novel cancer interventions for therapy and prevention*
4. *Foster training to ensure excellence within the IRP and to reflect the need for new, transdisciplinary approaches to cancer research*
5. *Implement a review and reward structure that will encourage innovation and collaboration, while maintaining a premium on scientific excellence*

IRP Reengineering Objective: 1

Objective 1 is to *define and enhance the value added of the Intramural Research Program.*

This objective encompasses the following aims:

1. *Preserve and enhance an environment conducive to innovative, high-risk, long-term basic research that will foster translational, clinical and population-based research*
2. *Identify functional structures within the IRP that facilitate interactions and collaborations across disciplines and among investigators in the various segments of the Intramural research community*
3. *Create an Intramural Research Program without walls to increase interactions and collaborations with extramural investigators*
4. *Expand interactions with the public and private sectors*

Preserve and enhance an environment conducive to innovative, high-risk, long-term basic research

- The major objective of re-engineering the Intramural Research Program is to enhance an environment conducive to innovative, high-risk, long-term basic research that leads to translational, clinical, and population-based research.
- The current excellence in basic research in the IRP provides the foundation upon which the IRP can establish a leadership role in transdisciplinary translational research.

Identify functional structures w/in the IRP that facilitate interactions...

- The IRP will continue to assess the appropriateness of current organizational structures
- Laboratories and Branches will continue to serve as the main administrative organization
- The IRP will build upon the success of the Faculties and Working Groups
- A disease-based, translational research matrix may be used to identify the intersection of programmatic translational research areas and opportunities in a particular cancer

NCI Faculties & Working Groups

Faculties provide a forum for scientists to engage one another to promote interaction and communication. Their goals are to:

- Promote translational and interdisciplinary research
- Develop new technologies and resources
- Enhance mentoring, recruitment and training of fellows
- Improve communication through retreats and seminars
- Sponsor visiting scientists
- Provide strategic planning and oversight
- Advise NCI leadership on important and innovative programs critical to the success of the NCI Intramural Program

24 IRP Faculties and Working Groups

Disease-based Faculties/Working Groups

Breast Cancer

Lung Cancer and Upper Aerodigestive

Cutaneous Carcinogenesis Working Group

Lymphoid Malignancy Working Group

Gynecologic Malignancies

Genitourinary Malignancies

Gastrointestinal Malignancies

Discipline-based Faculties/Working Groups/Initiatives

HIV and Cancer Virology

Cellular, Molecular, and Developmental Biology

Chemistry and Structural Biology

Epidemiology and Carcinogenesis

Nanotechnology Working Group

Immunology

HPV Working Group

Vaccine Working Group

Cancer Prevention

Metastasis Working Group

Approach-based Faculties/Working Groups

Genetics, Genomics, and Proteomics

Bioinformatics, Biostatistics

and Computational Biology

Clinical Immunotherapy

Molecular Targets

Vascular Biology

Integrative/Systems Biology

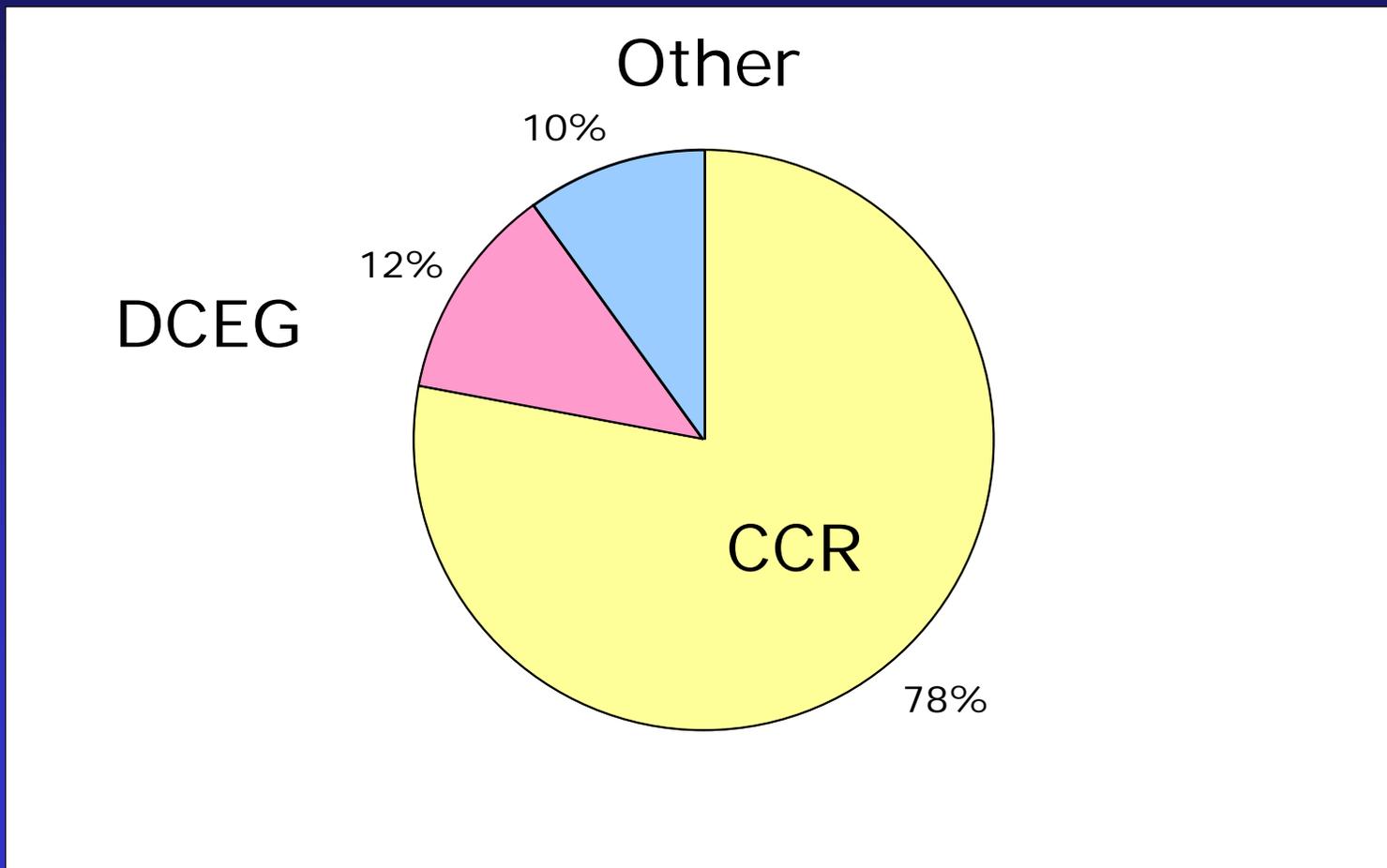
Stem Cell Working Group

Participation in Faculties and Working Groups

Number of Faculties/WG	Number of Members	Number of Steering Committee Members
24	1478	236

Faculty/Working Group Steering Committee Membership

174 Individuals are SC Members



Create an IRP “Without Walls”...

- A critical component of an IRP without walls is the establishment of mechanisms to foster the exchange of ideas among intramural and extramural scientists and clinicians.
 - *Encourage Consortium Development (LLMPP, Glioma, etc...)*
 - *NCI Distinguished Clinician-in-Residence*
 - *NCI Distinguished Scientist-in-Residence*
 - ***NCI Eminent Scholars***
 - *NCI Clinical Development Partnerships*
 - *NCI Advanced Technology Program*
 - ***NCI PI Sabbatical Program***

Create an IRP “Without Walls”...

–NCI Eminent Scholars

- Michael Sporn
- Mauro Ferrari

–NCI PI Sabbatical Program

- Howard Young
- Yves Pommier
- Samir Khleif

Expand Interactions...

- Several types of collaborative research relationships and partnership agreements with other government agencies, academia, and private sector organizations will be required for the Intramural Research Program to maximize benefit from the re-engineering.

NCI, CCR ---- A Track Record of Success.... (Active Collaborations with over 85 Organizations)

Abgenix Incorporated
Achillion Pharmaceuticals
Affymetrix
Agracetus/Auragen/Geniva/Powderject
AlbaPharm, Inc.
Amgen
Apoptogen, Inc.
Arcturus Engineering, Inc.
Aronex Pharmaceuticals, Inc.
Aventis
Baker Norton Corporation
Battelle Pulmonary Therapeutics, Inc.
Bayer Corporation
Beecher Company
Beiersdorf A
Beth Israel Deaconess Medical Center
Biogen, Inc.
Biomira USA, Inc.
Biovest International, Inc.
BMS/Clairol, Inc.
Boehringer Mannheim GmbH
Bristol-Myers Squibb
Cel-Sci Corp
Celgene Corp
Chiron Corp
Collgard Biopharmaceuticals, Ltd.
Connaught Tech. Corp. of Aventis
Eli-Lilly & Company
EntreMed, Inc.
Favril, Inc.
FibroGen, Inc.
Fujisawa HealthCare, Inc.

Genaissance Pharmaceuticals
Dyax Corp.
20/20 Gene Systems, Inc
Genentech, Inc.
Genetics Institute, Inc.
Genta, Inc.
Genzyme Corporation
Cenzyme Transgenics Corp.
GlaxoSmithKline
HybriVax Incorporated
ICOS Corporation
IDEC Pharmaceuticals
ILEX Pharmaceutical, LP
ImClone Systems, Inc.
Immunex Corp.
IntroGene BV
Intronn, Inc.
Isis Pharmaceuticals, Inc.
Janssen Research Foundation
Kimeragen
Medtronic AVE, Inc.
MITOS, Inc.
Monsanto Company
NeoPharm, Inc.
NeoRx
Nestec, Ltd.
NitroMed, Inc.
Merck
Millennium Pharmaceuticals
Novartis Pharma AG

Panacos Pharm, Inc.
Peregrine Pharm, Inc.
Pharmacia & Upjohn S.p.a.
Pharmagenesis
Philips Medical Systems
Nederland BV
Roche Diagnostics GmbH
Royal Free Hospital School
Medicine
Sanofi-Synthelabo Research
Schering-Plough Research
Institute
Seattle Genetics, Inc.
Shearwater Corporation
SmithKline Beecham
The Institute for Genomic
Research (TIGR)
Therion Biologics Corp.
U.S. Bioscience
Vical Incorporated
Vion Pharmaceuticals, Inc.
Vysis, Inc.
Warner-Lambert Company
Wyeth Lederle-Praxis Biologics
Wyeth-Ayerst Res., Inc.
ZymoGenetics, Inc.

IRP Reengineering Objective: 2

Objective 2 is to *develop innovative new technologies and approaches for cancer discovery, prevention, detection, diagnosis, and treatment.*

Four Centers of Excellence were established to support the IRPs dedication to high-risk, innovative basic, clinical, and epidemiologic research.

Advanced Biomedical Technology

– *J. Carl Barrett*

Molecular Epidemiology

– *Joseph F. Fraumeni, Jr.*

Immunology

– *Kathryn C. Zoon*

Medical/Molecular Oncology

– *Chief of Medicine, Recruit*

Centers of Excellence

- A Center of Excellence is a focus of resources and infrastructure with the purpose of accelerating the discovery, development, and delivery of interventions for the therapy or prevention of cancer.
- The Leader of the Center of Excellence:
 - serves as a steward of resources and infrastructure
 - facilitates interactions among NCI PIs and with other Institutes, extramural investigators, and the private sector
 - provides leadership and facilitates new initiatives

Advanced Biomedical Technology Center of Excellence

PROGRAMS

- Biomedical Proteomics Program
- Molecular Imaging Program
- Tissue Array Research Program
- Molecular Targets Development Program
- Comparative Oncology Program

UNITS

- Genome Analysis Unit
- Antibody and Protein Purification Unit
- Comparative Molecular Pathology Unit

INITIATIVES

- Animal Models Initiative
- RNAi Initiative
- Nanotechnology Initiative

CORES

- Microarray Core Facility
- Comparative Molecular Cytogenetics Core
- FACS Cores
- Confocal Cores
- SAIC Research Technology Program and Core Support
 - Advanced Biomedical Computing Center
 - Laboratory of Proteomics and Analytical Technologies
 - Protein Expression Laboratory
 - Protein Chemistry Laboratory
 - Laboratory of Molecular Technology
 - Microarray/Genomics
 - Image Analysis Laboratory

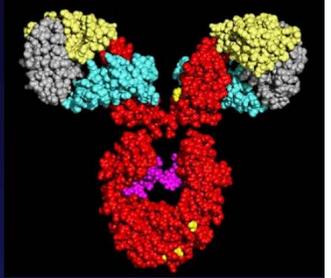
Molecular Epidemiology Center of Excellence

- Capitalize on the concentration of epidemiologists, clinicians, and biologists at NCI to form interdisciplinary research teams that address key questions in cancer induction and progression, thereby shaping new interventions
- Emphasis placed on integrating genomic and other emerging technologies into large-scale population studies to identify susceptibility genes and environmental interactions
- Encourage partnerships across NCI and with extramural community in building foundation for strategic coalitions

Molecular Epidemiology: Strategic Coalitions

- ***Cohort consortium:*** Coordinated series of parallel and pooled studies of more common cancers in population cohorts.
- ***Case-control consortia:*** Complementary strategy involving population-based and hospital-based case-control studies of less common cancers
- ***Family-based consortia:*** Discovery of rare high-penetrant genes plus their genetic and environmental modifiers
- ***International Research:*** Partnerships with NCI and other organizations to target studies.
- ***High throughput Genotyping:*** The Core Genotyping Facility performs high-throughput genotyping and sequencing to support genetic analysis for a broad range of projects.
- ***SAIC Research Technology Program (RTP) and Core Support:*** Centralized facilities for technology development and delivery to provide support for population studies of cancer risk.

Immunology Center of Excellence



Mission Statement:

To accelerate basic, translational, and clinical immunologic research and foster the discovery, development, and delivery of novel immunologic approaches for the prevention and treatment of cancers or viral infections that contribute to cancer.

Focus:

- Cell and Molecular Immunotherapies
- Vaccines
- Antiviral agents
- Immune-based product discovery, development, and delivery
- Research to identify new targets and approaches

Medical/Molecular Oncology Center of Excellence

- Medical Oncology Clinical Research Unit (MOCRU)
- Clinical Proteomics and Genomics
 - Serum Proteomics Reference Labs
 - Lysate antibody arrays
 - Clinical Microarrays
- Molecular Imaging Program
- PK/PD Clinical Core Facilities

Initiatives:

- Phase I Coordinating Committee
- Molecular Therapeutics Program
 - Preclinical Models Strategy Team

IRP Reengineering Objective: 3

Objective 3 is to *facilitate the development of a unique clinical research program in the IRP for delivery of novel cancer interventions for therapy and prevention.*

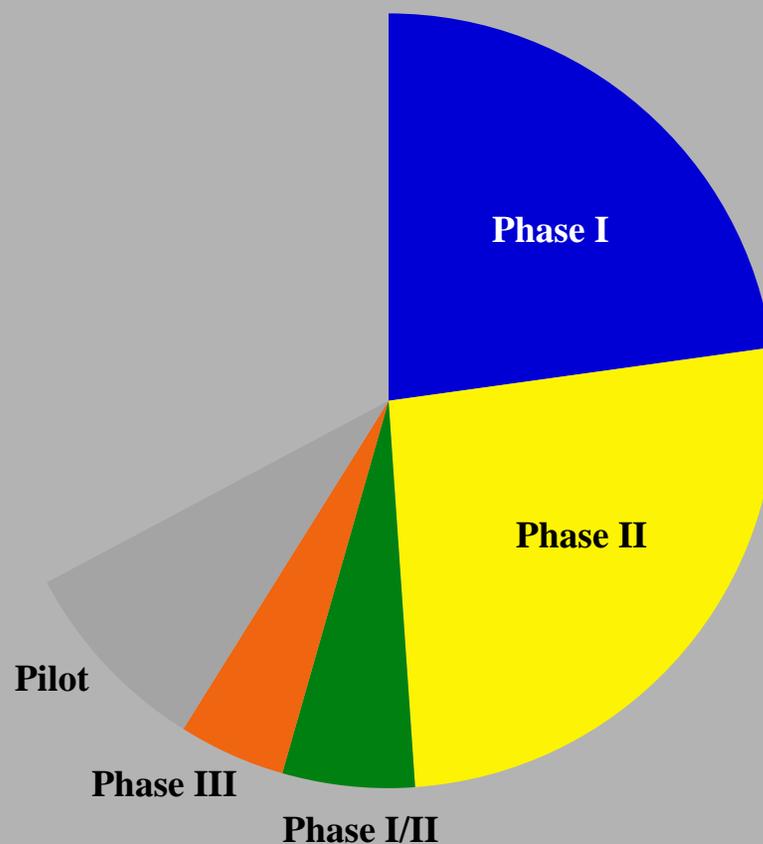
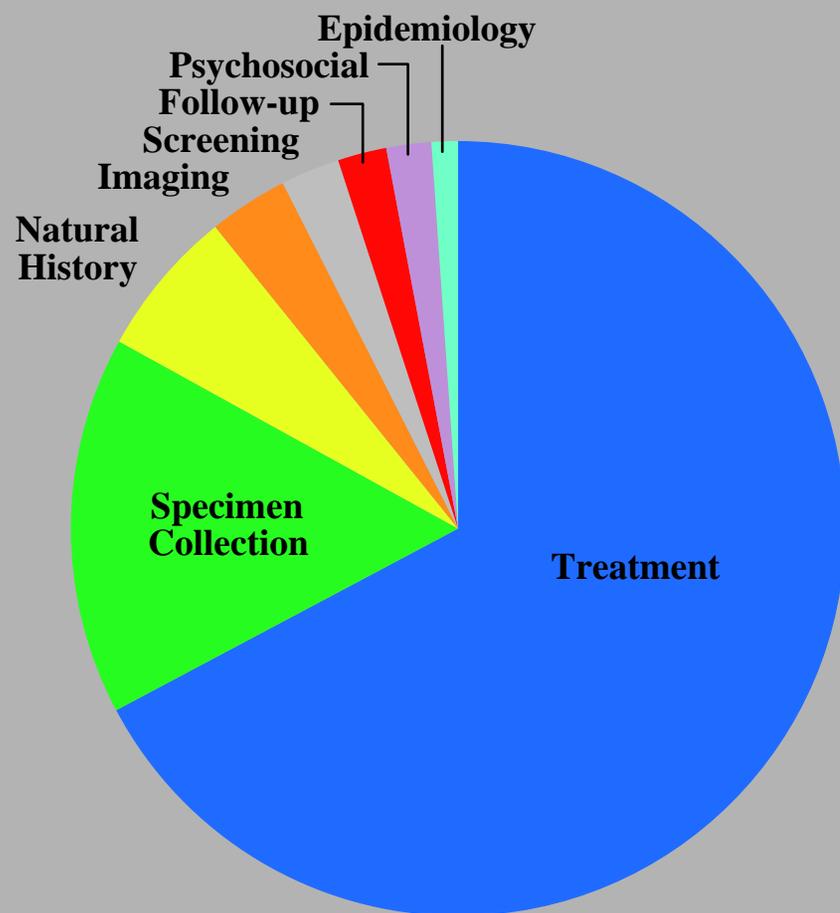
The aims of this objective include:

- Developing novel cancer interventions, novel ways to deliver effective interventions and novel methods to detect and diagnose cancer. (Clinical Research Program)
- Building a premier cancer research center that pioneers novel approaches to translational and clinical research through its basic and population-based research strengths
- Priority setting for NCI CCR clinical trials

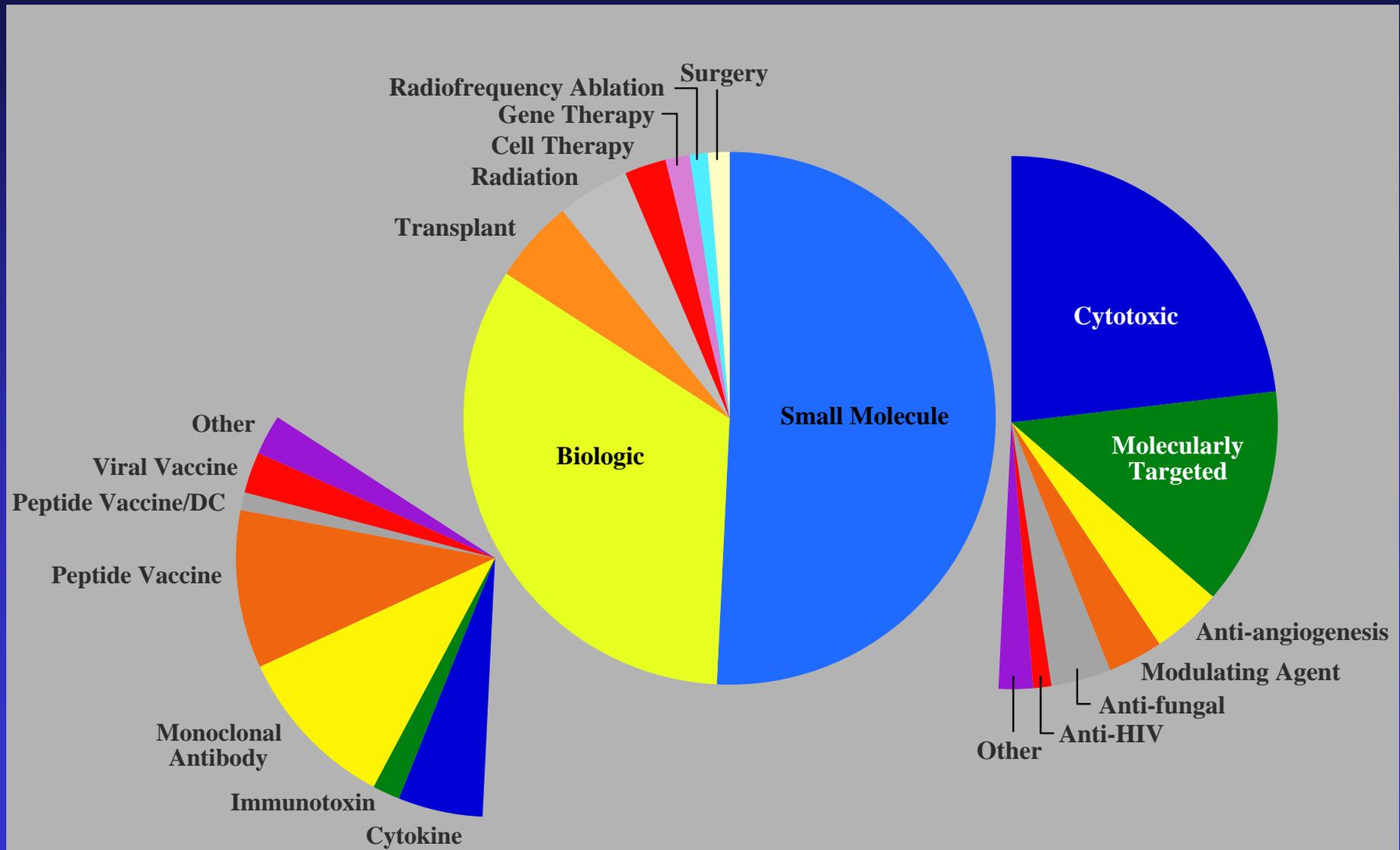
Centralized Clinical Trials Infrastructure

- Biostatistics
- Protocol administration/tracking
- Education and training
- Data management
- Quality control/quality assurance
- Patient outreach and accrual
- Informatics

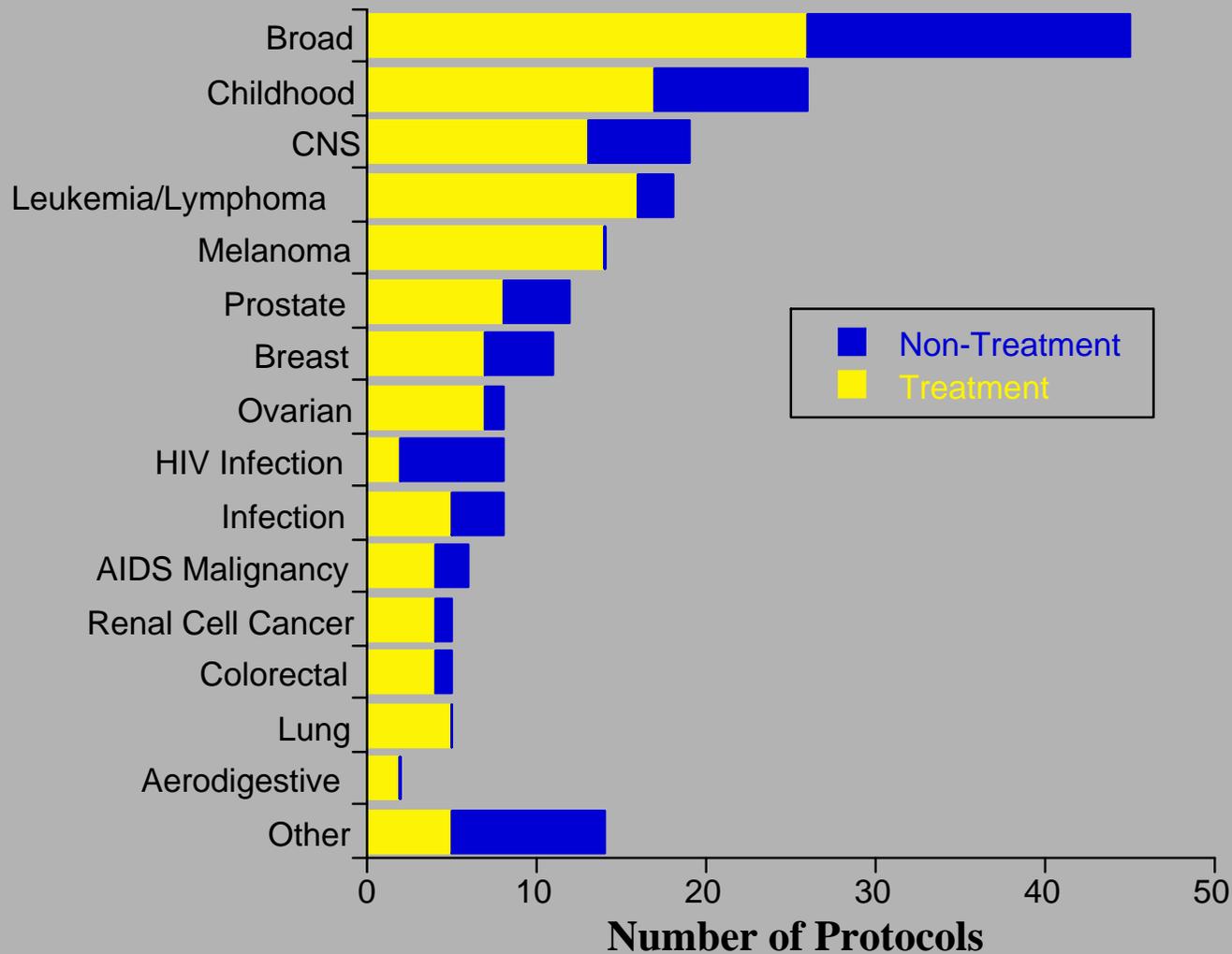
Categories of Open Clinical Trials



Open Treatment Trials by Modality



Open Clinical Trials by Disease



Medical Oncology Clinical Research Unit (MOCRUC)

Mission:

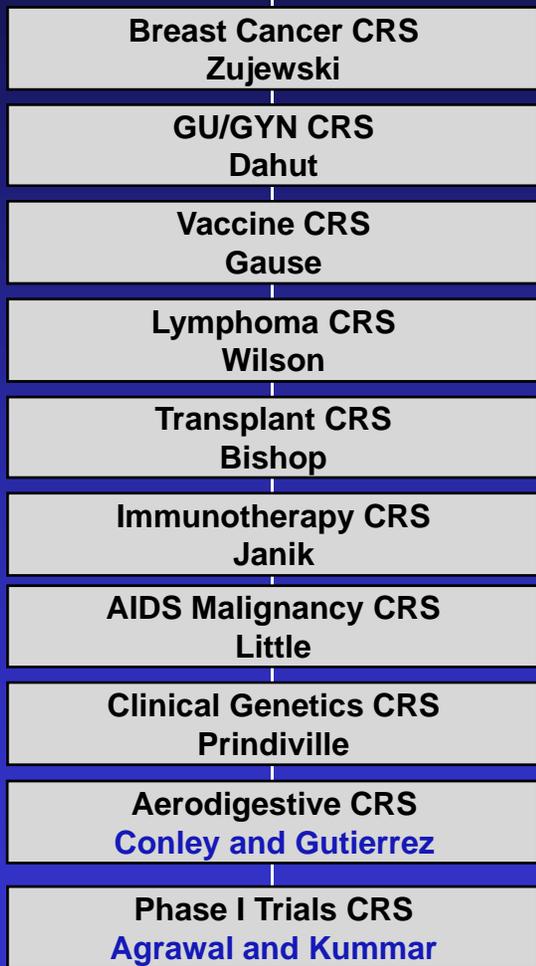
- To act as a clinical partner to all intramural PIs
- To facilitate the delivery of laboratory discoveries into the clinical setting
- To establish standards of excellence for clinical research and patient care

Excellence in three primary areas:

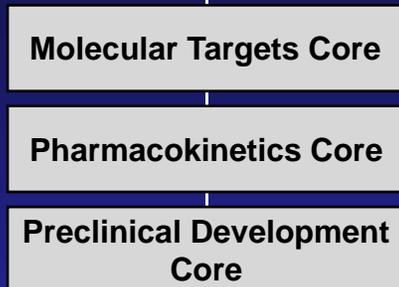
1. **Clinical research:** access to clinical research infrastructure, access to collaborators and/or advisors, formal scientific review of ideas, standardization of clinical research procedures for PIs and research nurses.
2. **Clinical care:** administration for inpatient and outpatient care services, core of dedicated clinical personnel to support all patient care activities.
3. **Clinical training:** administration of the medical oncology fellowship program, setting for optimal training, guidance for fellows.

Medical Oncology Clinical Research Unit (MOCRU)

Clinical Research Sections (CRS)



Cores



Offices



MOCRU: Year Two

- Recruitment of individuals to form senior staff clinical core - **done**
- Substantial changes in inpatient attending service - **done**
- Task force on outpatient clinic - **done**
- Formation of integrated clinical research teams - **done**
- Further changes in fellow recruiting - **done**
- Expansion of NP role in research and clinical care - **done**
- Re-evaluation of role of Navy component - **reorganization complete**
- Turn from structure/rules/people to function: vision - **ongoing**

IRP Reengineering Objective: 4

Objective 4 of the Re-engineering the Intramural Research Program document is *to foster training to ensure excellence within the IRP and to reflect the need for new, transdisciplinary approaches to cancer research.*

The aims of this objective included:

- Providing traditional basic, clinical and epidemiology research training as well as interdisciplinary and translational research training
- Offering trainees access to novel approaches and cutting-edge technologies
- Providing an environment for trainees where they have access to multiple mentors who have expertise in diverse fields of study
- Increasing interactions with the extramural community, provide improved training for graduate students, fellows and young investigators, and assist scientists in achieving their career goals

Training

- Outstanding training and an excellent training environment are essential for developing national leaders in cancer research and for distinguishing the IRP
- The IRP provides:
 - traditional basic, translational, clinical and epidemiology research training
 - trainees access to novel approaches and cutting-edge technologies such as imaging, nanotechnology, and computational biology
 - an environment for its trainees where they have access to multiple mentors who have expertise in diverse fields of study
 - an environment in which the skills necessary to effectively mentor the next generation of trainees can be learned

IRP Education Offices

- **DCEG Office of Education**

Established in 1999 it manages educational and training-related activities, including fellowship program, collaborates and coordinates with other NCI and NIH training offices, and fosters new collaborations and training opportunities in cancer epidemiology with academia

- **CCR Office of Education and Training**

Established in November 2001 it has a programmatic impact on the overall training experience of the basic scientists and clinical fellows in cancer research.

DCEG Office of Education Initiatives

- NCI pilot TU2 RFA for GPP
- Mentoring working group; development of mentoring guidelines and annual workshop
- Annual mentor award
- Annual training plans (fellows, tenure-track)
- Alumnus directory
- “Careers in Epidemiology” seminars
- Laboratory rotations (CGF/Chanock, others)
- Clinical rotations (Henkart, others)
- Writing skills workshop (Sgambati)
- Pathology seminar series (Sherman)
- Visiting Scholars Program
- ASPH/ACE Workshop on Doctoral Education

Summary of CCR Training Activities

- Twelve Clinical Fellowship Programs
 - Three ACGME accredited Residency Programs
 - Four ACGME accredited Clinical Fellowship Programs
 - Five additional Clinical Fellowship Programs
- Four Fellowships Focused Towards Translational Research
- Two Basic Science Fellowship Programs
- CCR Postdoctoral Retreat
- Course/Workshop Development
 - TRACO (Translational Research in Clinical Oncology)
 - TASC (Take A Scientist to the Clinic)
 - Demystifying Medicine for PhDs
 - Drug Development Premier
- K22 Career Development Awards to Facilitate the Transition to Independence
- Graduate Partnership Program to attract interactions with Extramural Institutions
- Summer Intern Program

IRP Reengineering Objective: 5

Objective 5 is to implement a review and reward structure that will encourage innovation and collaboration, while maintaining a premium on scientific excellence.

The aims of this objective were to:

- Promote an environment that rewards investigators for their scientific creativity, collaborative interdisciplinary and multidisciplinary research, willingness to take risks, and trying novel research approaches.
- Continue to support investigators dedicated solely to basic, clinical, and epidemiologic research.
- Bring expertise from diverse areas together to solve a problem and recognize programs that cut across Labs, Branches, and Divisions creating interdisciplinary and multidisciplinary research teams.
- Reward individuals for their achievements and contribution to scientific excellence in the IRP.
- Support programmatic participation by establishing guidelines for the recognition, review and reward of investigators who participate in interdisciplinary and multidisciplinary research in the IRP.

Immediate Impacts of Reengineering

- Better coordination and interactions with IRP
- Accelerated development and implementation of new technologies
- Facilitation of translational research
- Improvement of clinical research program
- More connections with extramural NCI investigators
- New partnerships with industry
- Improvement of training