



NIH IRP Long Term Planning

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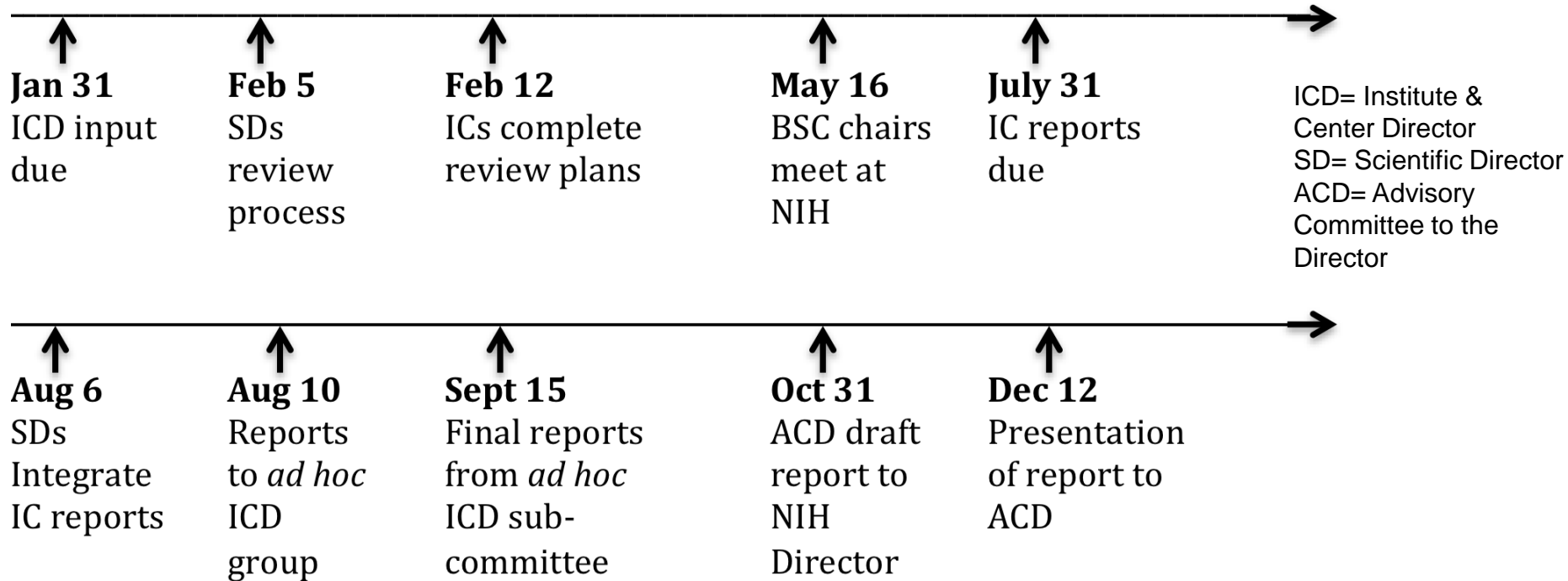
NCAB September 2014

- Early in 2014, Dr. Collins charged all ICs with developing a long-term plan with the broad goal of developing a ‘10 year vision’ for the NIH IRP
- Two major goals:
 1. Develop large-scale initiatives that capitalize on the distinctive features of the NIH IRP
 2. Develop a blue-print for maintaining scientifically distinctive and outstanding science within the NIH IRP- including a sustainable Clinical Research Center

NCI IRP Vision

- Support NCI's mission by identifying timely projects for broad collaborations across NCI's IRP
- Strengthen trans-NCI, trans-NIH collaboration
- Expand opportunities for collaboration with extramural investigators and/or industry
- Develop new ways to improve the use and fiscal health of the Clinical Center
- Identify new organizational elements and cultural features that further enhance the distinctiveness and success of the NIH IRP
- Identify barriers to achieving these goals

IRP Process



NIH IRP Long Term Planning Committee

Joan Conaway	Co-Chair	current BSC Chair
Louis Weiner	Co-Chair	current BSC Chair
Doug Lowy	Co-Chair	NCI
Ted Lawrence	Member	past BSC Chair
Liz Jaffee	Member	past BSC member/ current NCAB member
Ken Offit	Member	current BSC member
Margaret Spitz	Member	past BSA member
Jim Wells	Member	current BSC member
Bob Wiltrout	Member	NCI
Lee Helman	Member	NCI
Stephen Chanock	Member	NCI
Bob Hoover	Member	NCI
Crystal Mackall	Member	NCI
Tom Misteli	Member	NCI

- Each IC formed a review and planning committee composed of ~50% IC senior staff + ~50% BSC/extramural members



Current NCI IRP Staff

	Tenure Track PIs	Senior Investigators
CCR-Basic	29	124
CCR-Clinical	21	62
DCEG	27	44
Total	77	230

The number of PIs in the NCI IRP has been reduced by 18% from a high of 375 in 2002 to the current number of 307

180 departures and 113 new principal investigators

Active engagement with the two Board of Scientific Councilors (BSC)



Organization Membership

Organization	No. CCR Members/Fellows	No. DCEG Members/Fellows
National Academy of Sciences	8	1
Institute of Medicine	9	2
American Academy of Arts and Sciences	8	1
American Association for the Advancement of Science Fellows	20	1
American Academy of Microbiology	21	
Association of American Physicians	15	2
American Society of Clinical Investigation	23	2
NIH Distinguished Investigators	7	
American Epidemiological Society		15

Distinctive Features of NCI's IRP

- Size- nearly 30% of PI in the NIH IRP program are part of the NCI IRP
- The breadth and depth of its interdisciplinary science, which includes basic biology across multiple disciplines, clinical trials and the largest IRP population science effort
- The close geographic proximity of basic and clinical researchers in a “culture of the corridors” environment which facilitates bench to bedside to bench outcomes
- Disproportionate commitment to patient-based science that culminates in 35-40% of all clinical activity performed in the NIH Clinical Center, a unique venue that allows uncommon ability to perform intensive mechanistic studies
- Partnership with the Frederick National Laboratory for Cancer Research

Distinctive Features of NCI's IRP

- Supports a substantial number of commitments to long-term projects that would be difficult to sustain by standard extramural funding mechanisms
- **Strong commitment to the study of rare diseases, or diseases disproportionately afflicting underserved patient populations**
- Commitment to address challenging epidemiological questions, which are often pursued as a governmental function in most countries
 - Ability to respond to important mandates by access to large populations and the ability to move quickly to exploit opportunities provided by natural experiments wherever they occur throughout the nation or the world
- Charge to address questions in public health within the federal government, free from the constraint of revenue and profit

Some of Our Past and Ongoing Basic and Clinical Achievements

Enabled through collaboration and long-term commitment of resources and retrospective review

- Development of multiple FDA approved drugs for cancer and HIV
- Development of technology to enable HPV vaccine
- Contributions to understanding and treatment of rare cancers
- Key studies demonstrating success of adoptive immunotherapy of cancer
- Development of new, commercialized technology for imaging of prostate cancer
- Notable contributions:
 - Genetic susceptibility to kidney cancer leading to novel interventions
 - New insights leading to targeted interventions for lymphoma
 - Understanding of the role of chromatin structure and genome organization to cancer
 - Organization and regulation of the immune system, including the discovery of multiple key regulatory proteins

Creating New Opportunities

New competitive, time-limited funding options to support novel, high-risk and/or distinctive science

– **Major Opportunities Program**

- 3 ongoing projects (matrix drug screening; metabolic features of cancer; chromatin profiling)
- Projects aimed at accelerating development of innovative cancer treatment strategies by exploiting technological strengths within the CCR

– **Rare Tumor Initiative**

- Apply existing NCI expertise in basic and clinical studies of patients with rare tumors in the CC to identify and translate new therapies
- Pilot: Focused effort on desmoid tumors and plexiform neurofibromas (Widemann/Kummar)

– **New FLEX Programs**

- Series of new, competitive programs to support methods development, new intra-CCR collaborations
 - Methods and Technology Development Program
 - Synergy Award
 - “New Directions” Program
- To be launched fall/winter 2014

Clinical Research Priorities

- Design and execute novel, science-based clinical trials
- Take discoveries from within the CCR or other NIH laboratories to the point of first-in-human trials
- Focus on molecularly-based, tailored medicine
- Utilize technology and correlative science difficult to support elsewhere
- Foster the education and research of physician-scientists
- Study rare cancers that are not being adequately studied elsewhere



Areas of Clinical Strength

- NCI IRP will continue its active and growing programs in:
 - Lymphoma
 - Genitourinary malignancies (prostate, bladder and renal)
 - Neuro-oncology
 - Pediatric malignancies
 - Thoracic tumors
 - Marrow transplant
 - Immunotherapy
 - **Rare cancers**



Reengineering of the NCI's Clinical Research Program

- Major changes over the last few years:
 - Reorganization of Labs and Branches
 - Creation of Medical Oncology Clinical Service
 - Changes to protocol concepts and review
 - Accelerated the timeline for development and execution of clinical trials
 - Created a Protocol Support Office for Staff Training and Administrative Support in Protocol Development



Scientific Opportunities for Consideration

- 30 proposals received
- CSB reviewed all proposals
- 5 emerged for further consideration**
 - Precision Medicine and Prevention
 - Cell-based Therapies
 - The Human Microbiome
 - National Program for Natural Products Discovery
 - Human RNA Project

**All currently included in draft consolidated document for the NIH to the NIH Director's Advisory Committee to the Director

Precision Medicine and Prevention

Approach:

Develop PM strategies tailored to several pediatric and **rare cancers**, as well as several tumor types already prominently featured in the IRP portfolio

Exploit:

- access to well-characterized patient populations in the Clinical Center
- availability of molecular epidemiological datasets in DCEG
- strong expertise in molecular cancer mechanisms in CCR's basic science labs

Approach:

Drive a new wave of cell-based therapies by combining genome engineering, cell engineering and immunobiology

Goals:

Development of novel cell-based therapy approaches for:

- Cell therapy to common epithelial cancers using antigen identification with personal genomics
- Correction of monogenic disorders using genome engineering methods

Establish infrastructure for dissemination of cell-based therapies

- Focus on approaches and disease types that are not desirable for the current business plans of commercial entities, but which may inform future commercialization.

The Human Metaorganism in Cancer Biology and Medicine

Approach:

Focus resources and efforts to move the field from descriptive biology to mechanistic insight and metaorganism processes affecting cancer initiation, progression and therapy

Goals:

- Microbiome mapping in health and disease (genomic approaches)
- Mechanistic studies of microbiome function (inflammation, signaling, immune function)
- Microbiome in cancer treatment (susceptibility, progression, drug response, biomarkers)

National Program for Natural Products

Approach:

Contribute to a National Program for Natural Products Discovery for new molecules that target biological processes central to human disease --a national resource fully accessible to extramural investigators

Goals:

- Develop a comprehensive Natural Products Library (NPL) that includes:
 - pre-fractionated compounds (1 million) for modern high-throughput targeted screening technologies
 - analytical resources for isolation, structure elucidation, medicinal chemistry
 - public database and bioinformatics platform to integrate source organism, activity, structural, and genomic data
- Establish a national resource for Natural Products screening efforts for:
 - assay development
 - execution of natural product drug screens
 - resupply of active molecules
 - bioinformatics support to extramural users

The Human RNA Project

Approach:

Take leadership role in the development of a comprehensive program for the investigation and therapeutic exploitation of RNA

Goals:

Use a strong foundation in molecular biology and synergy with other ICs for:

- Systematic mapping of the RNAome in health and disease
 - genome-wide sequencing of mRNAs and unconventional RNAs
 - synergy with Precision Medicine data collection
- Elucidation of RNA structure
 - develop and apply methods to determine RNA structure (SHAPE, SAXS)
- Development of RNA-based therapeutic approaches
- Development of new clinical targets and trials

Next Steps

- **CCR planning series of workshops on each of these 5 topics this spring**
 - To include extramural experts
- **Clear opportunity to partner with extramural programs on rare tumors**
 - Would like to engage specifically in Precision Medicine workshop
- **Other opportunities?**