

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE
5TH JOINT MEETING OF THE BOARD OF SCIENTIFIC ADVISORS
AND THE NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
June 24, 2015**

**Building 31C, Conference Room 10
National Institutes of Health
Bethesda, Maryland**

**BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
June 24, 2015**

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 5th Joint Meeting on 24 June 2015, in Conference Room 10, C Wing, Building 31, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, 24 June 2015, from 8:30 a.m. to 4:25 p.m., and closed to the public from 4:30 p.m. to 5:30 p.m. The NCAB Chair, Tyler E. Jacks, Director, Koch Institute for Integrative Cancer Research, David H. Koch Professor of Biology, Massachusetts Institute of Technology, presided during the open session. In the absence of Dr. Todd R. Golub, Chief Scientific Officer, The Broad Institute of Harvard University and Massachusetts Institute of Technology, Dr. Jacks served as the *pro tem* Chair of the BSA. Dr. Jacks presided during the closed session.

BSA Members

Dr. Todd R. Golub (Chair) (absent)
Dr. Francis Ali-Osman
Dr. Kenneth C. Anderson
Dr. Dafna Bar-Sagi (absent)
Dr. Ethan M. Basch
Dr. Sangeeta N. Bhatia
Dr. Andrea Califano (absent)
Dr. Arul M. Chinnaiyan (absent)
Dr. Curt I. Civin
Dr. Graham A. Colditz (absent)
Dr. Chi V. Dang
Dr. Joseph M. DeSimone (absent)
Dr. Daniel C. DiMaio (absent)
Dr. Brian J. Druker (absent)
Dr. Karen M. Emmons (absent)
Dr. Betty Ferrell
Dr. Stanton L. Gerson
Dr. Joe W. Gray (absent)
Dr. Chanita Hughes-Halbert
Dr. Theodore S. Lawrence (absent)
Dr. Maria E. Martinez
Dr. Luis F. Parada (absent)
Ms. Diane Zipursky Quale
Dr. Martine F. Roussel
Dr. Kevin M. Shannon
Ms. Mary L. Smith
Dr. Lincoln D. Stein
Dr. Bruce W. Stillman (absent)
Dr. Gregory L. Verdine (absent)
Dr. Cheryl L. Walker
Dr. Irving L. Weissman (absent)
Dr. Eileen P. White
Dr. Kevin P. White

NCAB Members

Dr. Tyler E. Jacks (Chair)
Dr. Peter C. Adamson
Dr. Deborah Watkins Bruner
Dr. Yuan Chang (absent)
Dr. David C. Christiani
Dr. Marcia R. Cruz-Correa
Dr. Kevin J. Cullen
Dr. Judy E. Garber (absent)
Dr. Elizabeth M. Jaffee
Dr. Beth Y. Karlan
Dr. Timothy J. Ley
Dr. Olufunmilayo F. Olopade
Dr. Mack Roach, III
Dr. Jonathan M. Samet (absent)
Dr. Charles L. Sawyers (absent)
Dr. William R. Sellers (absent)
Dr. Max S. Wicha

Alternate Ex Officio NCAB Members

Dr. Robert T. Anderson, DOE
Dr. Michael A. Babich, CPSC
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS
Dr. Richard Pazdur, FDA
Dr. Craig D. Shriver, DOD (absent)
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)
Dr. Richard J. Thomas, OSHA/DOL

President's Cancer Panel

Dr. Barbara K. Rimer (Chair)
Mr. Hill Harper (absent)
Dr. Owen Witte (absent)

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Douglas R. Lowy, Acting Director, National Cancer Institute
Dr. Jeff Abrams, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis
Dr. Lynn Austin, Executive Officer, Deputy Director for Management
Dr. Stephen J. Chanock, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Acting Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. James Doroshow, Deputy Director for Clinical and Translational Research
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Peter Greenwald, Associate Director for Prevention
Dr. Ed Harlow, Special Assistant for Science Planning
Dr. Toby Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Lee Helman, Acting Director, Center for Cancer Research
Dr. Warren Kibbe, Director, Center for Bioinformatics and Information Technology
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Glenn Merlino, Acting Scientific Director for Basic Research, Center for Cancer Research
Dr. Alan Rabson, Deputy Director, National Cancer Institute
Dr. Dinah Singer, Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis Staudt, Director, Center for Cancer Genomics
Dr. Ted Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Maureen Johnson, Executive Secretary, Office of the Director
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy

Liaison Representatives

Ms. Carolyn Aldige, Cancer Research and Prevention Foundation
Dr. Carolyn Best, American Urological Association
Ms. Paula Bowen, Kidney Cancer Association
Dr. Susan Braun, National Cancer Institute, Council of Research Advocates
Mr. William Bro, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Mr. Matthew Farber, Association of Community Cancer Centers
Dr. Margaret Foti, American Association for Cancer Research
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Ms. Shandi E. Hill, American Society of Therapeutic Radiology and Oncology
Ms. Ruth Hoffman, Candlelighters Childhood Cancer Foundation
Dr. Gerald F. Joseph, Jr., American College of Obstetricians and Gynecologists
Ms. Rebecca A. Kirch, American Cancer Society
Dr. Steven Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education
Ms. Christy Schmidt, American Cancer Society
Ms. Susan Silver, National Coalition for Cancer Survivorship

Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Ms. Pamela A. Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

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WEDNESDAY, JUNE 24, 2015

I. CALL TO ORDER AND OPENING REMARKS—DR. TYLER E. JACKS

Dr. Jacks called to order the 5th Joint BSA and NCAB meeting and welcomed members of the Board, *ex officio* members of the Board, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Dr. Jacks reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 11 March 2015 BSA meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DR. TYLER E. JACKS

Dr. Jacks called Board members' attention to future meeting dates.

Motion. A motion to confirm the future meeting dates for the BSA and NCAB for 2015 and 2016 was approved unanimously.

III. NCI DIRECTOR'S REPORT—DR. DOUGLAS R. LOWY

Dr. Douglas R. Lowy, Acting Director, welcomed and thanked members for attending despite the inclement weather across the United States. He provided an update on the status of NCI programs. Members were informed that the first recipients of the Outstanding Investigator Award (OIA) will be announced in the next few weeks. Dr. Lowy told members that the OIA provides long-term support to experienced investigators with outstanding records of cancer research productivity who propose to conduct exceptional research, and it allows them the opportunity to take greater risks, be more adventurous in their lines of inquiry, and take the time to develop new techniques.

Dr. Lowy reminded members that President Barack Obama has proposed \$70 million (M) in his fiscal year (FY) 2016 budget for the Precision Medicine Initiative in Oncology (PMI-Oncology). The NCI's approach to PMI-Oncology will be discussed later in the meeting, and a future workshop will explore the translational potential for the specific reactivation or replacement of tumor suppressor gene activities. PMI-Oncology concerns cancer screening and prevention, as well as treatment. Members were informed that the NCI is emphasizing screening based on application to molecular diagnostics, rather than pattern recognition. For example, in cervical cancer screening, cytologic or Pap smear screening is more sensitive for detecting squamous cell cancer precursors than for detecting adenocarcinoma precursors; a substantial decrease in squamous cell cancer incidence at the cervix has not been found in adenocarcinoma. A study published recently in *The Lancet*, which combined four randomized controlled trials conducted in Europe, found that human papillomavirus (HPV) testing can prevent more cervical cancers, especially adenocarcinomas, than cytology. Aspirin has shown similar results in reducing the risk of several cancers, particularly colorectal cancer. Molecular understanding can be used to risk-stratify those patients who will derive the greatest benefit from aspirin, thus increasing the benefit/harm ratio and addressing concerns about side effects of aspirin that have prevented its recommendation for reducing cancer risk. Members were reminded that the NCAB had previously heard data from Dr. Andrew Chan showing that high 15-hydroxyprostaglandin (15-HPGD) in the normal colon is associated with reduced risk of colorectal cancer in regular aspirin users.

Members were informed that another area of NCI interest is specific cancers with health disparities, as these represent high-risk populations. Dr. Lowy stated that the NCI will identify specific

cancers, such as colorectal, liver, breast, and prostate cancers; identify risk factors and their relative contribution to disparities, including biological and lifestyle factors, as well as health care access and utilization; and explore efforts to mitigate those risk factors. He referred to a study published in *Proceedings of the National Academy of Sciences (PNAS)* that found 15 novel recurrently mutated genes in colon cancer among African Americans, but not in Caucasians, suggesting an important difference in the mutational landscapes arising in various ethnic groups. Access to minority populations is important for such studies, and the NCI's efforts to include underrepresented minorities in the NCI Cooperative Group Clinical Trials during the past 5 years have resulted in approximately one in five patients being minority individuals.

Strong Support for Basic Research and the NCI Budget. Dr. Lowy emphasized the NCI's continued strong support for basic research that can elucidate important processes that lead to cancer. He described the declining purchasing power of the NCI budget, which had doubled between 1999 and 2004 and seen an appreciable increase in 2009–2010 because of the American Recovery and Reinvestment Act of 2009, which helped to support The Cancer Genome Atlas (TCGA) Project. In inflationary terms, however, the NCI's current purchasing power is similar to that of 1999. Dr. Lowy expressed cautious optimism about increases in appropriations for the NCI and NIH for FY 2016.

Members were told that 1,200 new competing research project grants were awarded in FY 2014, more than the 1,100 awards made in each FY 2012 and 2013, and that the NCI is committed to maintaining this number. Dr. Lowy noted that the appropriation to the NCI decreased 5 percent in FY 2013 because of sequestration. He described several financial and demographic changes instituted by the NCI, including a decrease in the automatic cuts to the modular R01 grants from 17 percent to 8.5 percent, and an increase in both the average size of the OIAs and their length, from 5 years to 7 years.

NCI-Designated Cancer Centers. Dr. Lowy remarked on the recommendations of the Cancer Centers Working Group and expressed the NCI's commitment to increase the total amount of the P30 core grants starting in FY 2016, with initial focus on the Centers with the lowest size grants and a long-term goal of increasing the funding pool from \$255 M to \$300 M.

RAS Project. Dr. Lowy informed members that the RAS Project, which is managed by the Frederick National Laboratory for Cancer Research (FLNCR), is producing validated gateway entry clones for 180 genes, or a total of 360 clones, of which 17 were not available commercially and 32 were not available without non-silent mutations. The clones will be made available to the community, and requests can be sent to Dr. Dom Esposito, FLNCR (espositod@mail.nih.gov).

FNLCR Recompetition. Dr. Lowy stated that the NCI has announced the recompetition for the Operations and Technical Support contract that runs the NCI Federally Funded Research Development Center known as the FNLCR. Leidos Biomedical Research currently administers the contract. Information concerning the competitive process will be announced on FedBizOpps and the FNLCR Acquisition Portal, with a pre-proposal conference scheduled for early October 2015. Members were told that the NCI will ensure a fair and open contract competition.

Personnel Changes. Members were informed of the retirements of Dr. Robert Wiltout, Director, Center for Cancer Research (CCR), in July; Dr. Joseph Tomaszewski, Co-Director, Division of Cancer Treatment and Diagnosis (DCTD), in May; and Ms. Susan Erickson, Office of Government and Congressional Relations (OGCR), in May. New appointments include Dr. Toby Hecht, Deputy Director, DCTD; Dr. Lee Helman, Acting Director, CCR; Dr. Glenn Merlino, Acting Scientific Director (Basic Section), CCR; Ms. M.K. Holohan, Acting Director, OGCR; and Mr. Peter Garrett, Director, Office of Communications and Public Liaison (OCPL).

Center for Global Health (CGH). Dr. Lowy introduced Dr. Marie Ricciardone, newly recruited to the CGH. Dr. Ricciardone is a molecular biologist who previously was a professor at Bilkent University in Ankara, Turkey, and whose husband served as the U.S. Ambassador to Turkey.

NCI Outreach. Members were referred to a new version of the NCI's website (www.cancer.gov), which is now compatible with smartphones, and were encouraged to review and share feedback on it. Dr. Lowy commended Dr. James H. Doroshow, Deputy Director, on the recent opening of the NCI-Molecular Analysis for Therapy Choice (NCI-MATCH) Trial and the notable media interest in the project. He also expressed appreciation for members' input and reflected on the importance of the NCI's work to help patients live longer, healthier lives by decreasing the incidence of cancer and improving the outlook for patients who develop cancer.

Questions and Answers

Dr. Jacks requested further information about the recompetition of the FNLCR. Dr. Lowy said that the Frederick National Laboratory Advisory Committee (FNLAC) has provided guidance about the direction of the FNLCR, influenced by a visit to the U.S. Department of Energy's (DOE) Lawrence Berkeley National Laboratory, which operates as a partnership between corporate and academic entities. Enthusiasm continues for FNLCR programs, including the RAS Project and NCI Experimental Therapeutic (NExT) Program.

Dr. Elizabeth M. Jaffee, The Dana and Albert "Cubby" Broccoli Professor of Oncology, Co-Director of the Gastrointestinal Cancers Program, and Associate Director for Translational Research, The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, asked about NCI's activities in cancer immunology and inflammation. Dr. Lowy recognized the importance of these areas for both the pathogenesis and treatment of cancer and expressed the NCI's aim to complement private-sector studies in these areas by elucidating immune and inflammatory mechanisms.

IV. PRESIDENT'S CANCER PANEL REPORT—DR. BARBARA K. RIMER

Dr. Barbara K. Rimer, Dean, Gillings School of Global Public Health and Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, provided a report on the recent activities of the President's Cancer Panel (PCP, the Panel). Dr. Rimer stated that the mission of the PCP is to identify barriers to progress of the National Cancer Program and communicate them to the President of the United States. In addition to Dr. Rimer, the Panel members include Dr. Owen N. Witte, University of California, Los Angeles, and actor Hill Harper. Dr. Rimer reported on outcomes stemming from the PCP's 2012–2013 Report to the President, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer," to which Drs. Lowy and Harold Varmus provided input, and the status of the current 2014–2015 workshop series, "Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes."

By working closely with a number of key organizations, such as the Centers for Disease Control and Prevention, the American Cancer Society and the National Vaccine Advisory Committee (NVAC), the PCP was able to secure commitments to a number of their recommendations before the report was released. A broad coalition of public, private, and voluntary organizations is collaborating to increase HPV vaccination coverage and agreed at the first meeting of the National HPV Vaccination Roundtable in February 2015 that all pilot projects implemented by the Roundtable must be responsive to the PCP's HPV report recommendations. In June 2015, the National Vaccine Advisory Committee (NVAC) approved the five recommendations of the NVAC HPV Working Group, which included endorsing the Panel's HPV report and adopting its recommendations. In addition, the NVAC HPV Working Group endorsed monitoring the uptake and implementation of PCP recommendations, and urged that the

Assistant Secretary for Health develop relevant communications strategies to increase HPV vaccine uptake. Members were informed that the NCI is conducting intramural and extramural research on the HPV vaccine that is responsive to the Panel's recommendations. Dr. Lowy stated that another NVAC recommendation for a large-scale trial to evaluate two- and one-dose regimens of the two approved HPV vaccines would have benefits for costs, logistics, and uptake. Dr. Abby Sandler, NCI, will provide the keynote address on the PCP's HPV report at the November 2015 Cancer Prevention & Research Institute of Texas conference.

Members were informed that the PCP's 2014–2015 workshop series addresses the potential of connected health to improve cancer-related outcomes. Dr. Rimer explained that the workshop series included a planning meeting in June 2014, as well as workshops on engaging patients in Boston in December 2014 and on personal health data and cancer in San Francisco in March 2015. Participants at the workshops discussed opportunities provided by connected health to improve patient outcomes, the need for connected infrastructure to support team care and precision medicine, and the advantages of connected care in facilitating patient participation in clinical trials and diminishing disparities in care and health outcomes. A third workshop is planned for Chicago in July 2015 to identify recommendations to achieve a future state that would be beneficial to patients and the public by focusing on personal health information and data sharing, person- and family-centered care, optimal use of devices, and the National Health Information Infrastructure, including opportunities to use patient-reported outcomes (PROs) in a proactive way. Dr. Rimer was joined by Dr. Brad Hesse, Division of Cancer Control and Population Sciences (DCCPS), who described fractures in the foundations of cancer care that could be addressed by connected health, including: primary prevention (e.g., follow-up for smokers), secondary prevention (e.g., uptake of screening in the community health system), treatment adherence, and communication problems experienced by cancer survivors. Future stresses in oncology that may worsen these fractures include aging demographics, higher incidence rates, more complex oncology care, an increasing number of survivors, a shrinking workforce, and rising treatment costs. The health care communication revolution provides opportunities to bridge gaps by fixing patient handoffs, utilizing new communication technologies, smart scheduling, and secure messaging, and better leveraging eHealth to move care to patients. Members were told that following the 2014–2015 series of workshops, the PCP will review the input that it has received, conduct additional research as needed, and prepare a report to the President.

Questions and Answers

Ms. Mary L. Smith, Co-Founder, Research Advocacy Network, asked whether the ways in which behavioral change can be achieved had been discussed. Dr. Rimer confirmed that behavioral change had been part of the discussions.

Dr. Ethan M. Basch, Associate Professor of Medicine, Division of Hematology/Oncology, and Director, Cancer Outcomes Research Program, The University of North Carolina at Chapel Hill, observed that connected health offers opportunities to leverage tools developed from research, as well as to use tools from clinical practice in research, such as the NCI Patient-Reported Outcomes Measurement Information System (PROMIS). He also noted the need for quality metrics to assess engagement and connectivity of patients with providers and between the research and patient worlds. Dr. Rimer agreed and said that research tools, such as visualization, could be valuable for patients and their doctors to track progress; quality metrics also are needed, and the effects of social media should be studied. Dr. Hesse added that connected health provides opportunities to locate the breakdown points in patient care.

V. CENTER FOR CANCER RESEARCH AND FOOD AND DRUG ADMINISTRATION COLLABORATION—DR. RICHARD PAZDUR

Dr. Richard Pazdur, Director, Division of Hematology and Oncology Products, U.S. Food and Drug Administration (FDA), presented a joint FDA-NCI program to recruit clinical investigators who will perform clinical and regulatory duties for the two organizations. Dr. Pazdur was joined by fellow presenters, Drs. Sanjeeve Balasubramaniam, FDA; and Lee Helman, Scientific Director for Clinical Research, CCR. The program is to fill positions that will be joint appointments at the CCR and FDA's Center for Drug Evaluation and Research (CDER)/Office of Hematology and Oncology Products (OHOP). Members were informed that investigators will be FDA employees and will become expert in regulatory processes focusing on a specific disease type, from the Investigational New Drug (IND) application to the non-disclosure agreement (NDA) and post-marketing, and will develop a pivotal role in guiding industry and academia in their approach to drug development. At the NCI, the investigators will collaborate with existing clinical teams in the development and execution of clinical trials, the enrollment of patients, and the analysis and publication of data, as well as serve as a sounding board for clinical trial design. Mid-career clinical investigators with clinical trial experience are sought, particularly those with expertise in a particular disease area in hematology/oncology and interest in maintaining an active clinical research career while developing regulatory expertise in oncology. Dr. Balasubramaniam stated that in response to changes in the clinical regulatory pathway, which now include pharmacodynamics evaluation and biomarkers (Phase 0), safe dose (Phase 1a), dose expansion for specific populations (Phase 1b), and randomized accelerated approval (Phase 2), the OHOP reorganized in 2011 into disease-specific divisions to better support clinical trial design and facilitate a new drug development environment.

Members were told that the joint position will include titles from both organizations. An Associate Director at the OHOP receives regulatory training within the context of a multidisciplinary, disease-specific team; oversees a portfolio of drug and biologic products at all phases of development; leads meetings with industry and academic sponsors; represents the FDA to external stakeholders; and can conduct and publish regulatory science using the FDA's data and computing resources. Dr. Helman stated that a principal investigator (PI) at the CCR will collaborate within the Center; develop and submit clinical trials; conduct an estimated two to four actively accruing clinical trials; teach; and conduct investigator-initiated, industry, and cooperative group studies. Members were informed that the CCR includes 15 clinical oncology branches and provides substantial support throughout a protocol lifecycle, as well as support for technology transfer partnerships, research nursing, clinical care, core facilities, basic science, and data management.

Dr. Balasubramaniam stated that FDA/CCR clinical investigators would serve as leaders in the academic community, bringing disease-specific expertise, fulfilling unmet clinical needs at the FDA, and advancing efforts to modernize clinical trial design to align with the clinical community. Investigators would help the NCI design trials that establish and use new regulatory endpoints, such as alternatives to current surrogates or dose-finding schema, as well as expand inclusion criteria and highlight regulatory considerations in individual trials. Members were told that the FDA will serve as the chair of the search committee, and the CCR will participate in the search and selection of investigators.

Questions and Answers

Dr. Peter C. Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, wondered about the challenges in recruitment and retention of investigators at the mid-career level. Dr. Pazdur said that the ideal candidate would be an established investigator with a presence in a specific field. He added that the clinical work in the joint position ensures that it is remarkably different from other career positions at the FDA.

Dr. Max S. Wicha, Deputy Director, Taubman Institute, Distinguished Professor of Oncology, and Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, encouraged the FDA and NCI leadership to consider the program as having a dual mission of training investigators who remain in the Federal Government for their career and those who leave for careers in the extramural community. Dr. Olufunmilayo F. Olopade, Walter L. Palmer Distinguished Service Professor of Medicine and Human Genetics, Associate Dean for Global Health, and Director, Center for Clinical Cancer Genetics, University of Chicago Pritzker School of Medicine, said that the efficacy of the training could be expanded by engaging extramural training programs.

Dr. Wicha suggested that recruiting experts in Phase 1 development would leverage the increased focus on immune therapies and pathways in drug development. Dr. Pazdur responded that recruitment is focused on finding the right candidate and not targeted to a specific cancer.

Dr. Stanton L. Gerson, Shiverick Professor of Hematological Oncology, Director, Case Comprehensive Cancer Center, Director, National Center for Regenerative Medicine, Case Western Reserve University, and Director, Siedman Cancer Center, University Hospitals Case Medical Center, encouraged the FDA and NCI leadership to stress that this program will help develop a leading edge competency in technologies and approaches that could not be achieved otherwise.

VI. RECOGNITION OF RETIRING BSA MEMBERS—DR. DOUGLAS R. LOWY

On behalf of the NCI, Dr. Lowy recognized the contributions made by members of the BSA whose terms of office have expired. He expressed appreciation for their service and dedication over the course of their terms. Retiring BSA members are: Drs. Curt I. Civin, Director, Center for Stem Cell Biology & Regenerative Medicine, Professor of Pediatrics & Physiology, and Associate Dean for Research, University of Maryland School of Medicine; Betty Ferrell, Professor, Nursing Research and Education, Full Member, Cancer Control and Population Sciences Program, Comprehensive Cancer Center, City of Hope National Medical Center; Todd Golub, Chief Scientific Officer, The Broad Institute of Harvard University and Massachusetts Institute of Technology; Bruce W. Stillman, President and Chief Executive Officer, Cold Spring Harbor Laboratory; and Irving L. Weissman, Director, Institute of Stem Cell Biology and Regenerative Medicine, Stanford University.

VII. NCAB PHASE II CANCER CENTERS BUDGET WORKING GROUP REPORT—DR. STANTON L. GERSON

Dr. Gerson presented the findings in the NCAB Cancer Centers Working Group Report, Phase II: Streamlining the Cancer Center Support Grant (CCSG) Application and Evaluation Process. In its report, the Working Group—composed of nine Center Directors, four Associate Directors, and three NCI staff—aimed to improve and enhance the CCSG application and review process, amplify referees' ability to understand the importance and innovation of the Centers, remove and reduce the administrative burden, and streamline the process of application review. The Working Group began preparations in April and May 2014; divided into four working groups, conducted team teleconferences, and engaged in email dialogue from June through August 2014; assembled the final report in September and October of 2014; discussed the report at the Subcommittee A "Parent Committee" meeting in December 2014; and presented the report at the Cancer Centers Director's meeting in February 2015.

Members were informed that the Working Group unanimously approved the final report, which developed recommendations in four major areas. (1) Regarding the value and efficiency of the site visit, the report observed that other mechanisms do not have site visits, eliminating site visits would represent a significant time and cost savings for Centers and the NCI, and the scoring impact may balance out the results of the site visit. The report recommended eliminating site visit tours and poster presentations for

Shared Resources and replacing them with a question-and-answer session for Shared Resources. The Parent Committee reiterated the team-building value of the site visit for Centers and the opportunity provided by the site visit to answer questions better than written documentation. (2) Regarding clarity of the requirements and review criteria, the report recommended eliminating redundancy in the requirements for submission and review, restoring individual review of Shared Resources, and better defining eligibility requirements for the “comprehensive” designation to increase understanding by the Centers and reviewers. The Parent Committee commented that redundancy has some value for reviewers, individual review of Shared Resources is preferred, and added specificity may constrain Centers and reviewers. (3) The report recommended streamlining data collection by making greater use of direct data acquisition methods, progress on which is already occurring through the use of existing systems, such as the Clinical Trials Reporting Program (CTRP) and Research Portfolio Online Reporting Tools Expenditures and Results (RePORTER); and using electronically available resources for biosketches. (4) To streamline annual CCSG progress reports, the report recommended simplifying the process by reducing their length and providing annually updated Data Tables to track progress. Dr. Gerson indicated that next steps include implementing changes to elements not defined in the CCSG funding opportunity announcement (FOA) and addressing other issues at the CCSG FOA reissue in September 2016.

Questions and Answers

Drs. Chi V. Dang, Professor of Medicine, Division of Hematology-Oncology, Department of Medicine, Director, Abramson Cancer Center, and Director, Abramson Cancer Research Institute, Perelman School of Medicine, University of Pennsylvania, and Kevin Shannon, Roma and Marvin Auerback Distinguished Professor in Molecular Oncology, American Cancer Society Research Professor, Department of Pediatrics, University of California, San Francisco, encouraged the NCI to provide guidance regarding the type of data or other content that would be most valuable to include in the Cancer Centers’ progress reports to better support the NCI’s mission.

Members expressed support for the inclusion of the site visit in the evaluation process as a means to galvanize the Cancer Centers. Dr. Kevin J. Cullen, Director, Marlene and Stewart Greenbaum Cancer Center, Professor of Medicine, University of Maryland, observed that the site visit provides an impetus to focus investigators and program members within a Center on the broader landscape and positively affects the science that the Center produces. Dr. Cheryl L. Walker, Professor and Director, Institute of Biosciences and Technology, Center for Translational Cancer Research, and Welch Chair in Chemistry, Texas A&M Health Science Center, stressed the importance of onsite team interactions, as virtual reviews become more prominent.

Dr. Wicha asked why the site visit was made optional in the review process. Dr. Gray explained that several Cancer Centers previously had felt that they could go through the peer review process without the site visit; these Centers have since indicated that they would prefer having the site visits. Dr. Lowy stated that the NCI would be willing to implement changes provided that the review process remained rigorous and fair.

Dr. Adamson queried about refinements to the goal of the site visit, and Drs. Jacks and Gray responded that the site visit could be perceived as a part of the evaluation of the application. Dr. Gerson added that while site visits can help to improve applications, they should not be used to correct deficiencies. Dr. Dang confirmed that the Cancer Centers Working Group discussed whether the score before a site visit and after a site visit may have a substantive change or not.

Dr. Jaffee asked about ways to enhance the value of the site visit. Dr. Gerson responded that the Working Group had requested that the NCI help it to understand the value of the site visits and which parts are of most value.

Motion. A motion to express support that site visits be a mandatory part of the evaluation of NCI-designated Cancer Centers was approved with 30 ayes, 1 nay, and 1 abstention.

Motion. A motion to accept the report of the NCAB Phase II Cancer Centers Working Group Report was unanimous.

VIII. PRECISION MEDICINE INITIATIVE—DRS. JAMES H. DOROSHOW, LOUIS M. STAUDT, AND WARREN KIBBE

Dr. Doroshow provided an overview of the PMI-Oncology activity announced in President Obama's 2015 State of the Union Address. The President's Budget for FY 2016 allocates to the NCI a \$70 M net increase for its PMI activities, which focus on using genomics to identify and target molecular vulnerabilities of individual cancers. The PMI has four major goals: (1) expand genomics-based clinical and preclinical studies; (2) overcome, at the molecular level, resistance to targeted drugs and gain a mechanistic understanding of immunotherapy; (3) develop a large-scale, patient-derived, clinically annotated repository for evaluating targeted therapeutics; and (4) establish a national cancer database to integrate genomic information with clinical response and outcome. Dr. Doroshow informed members that a series of precision oncology trials were initiated in 2014: Molecular Profiling-Based Assessment of Cancer Therapy (NCI-MPACT); Lung Cancer Master Protocol (LungMAP); Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST); and Exceptional Responders. NCI-MATCH, a foundational trial that attempts to discover whether cancer treatment can be assigned based on molecular abnormality, launched in 2015 and will be available at 2,400 sites across the United States and also will serve as a regulatory umbrella. The NCI-MATCH trial is available for solid tumor patients and patients with non-Hodgkin's lymphoma; other immunologic malignancies will be added if resources become available. Future goals include establishing NCI-Pediatric MATCH and broadening the NCI-MATCH umbrella.

Dr. Louis M. Staudt, Director, Center for Cancer Genomics (CCG), elaborated on the need for precision medicine in oncology, noting that the current repertoire of cell lines is insufficient. Needed are patient-derived cancer models that recapitulate genotypes and phenotypes of human cancer cells to develop single and multidrug combinations that are specific to the characteristics of the tumors and to perform high-throughput small-molecule drug screening to identify new targets. Dr. Staudt expressed excitement about the accelerated pace of technological development for the study of functional dependencies. He noted that two new advancements—organoids and conditionally reprogrammed cells—hold promise for precision medicine. Dr. Staudt explained that the pilot phase of a human cancer model initiative would capture clinical data and produce, characterize, and make widely available new models. A 2-year contract is in place to create 1,000 new human cancer cell lines. The pilot has scientific, methodological, ethical, regulatory, and procedural considerations yet to be resolved, but a meeting to discuss operational details is planned for July 2015 at the NCI.

Dr. Warren Kibbe, Director, Center for Biomedical Informatics and Information Technology (CBIIT), described the Genomic Data Commons (GDC) and the NCI Cancer Genomics Cloud Pilots. The GDC is a single repository for all NCI cancer genomics data that will serve as a single platform for reharmonizing the data. Data will be freely available for download, subject to data access requirements. The NCI Cancer Genomics Cloud Pilots will explore approaches for meeting the research community's need to analyze large-scale cancer genomic and clinical data. The Cloud Pilots offer an opportunity to establish sustainable infrastructure, provide a data integration platform, and support clinical research focused on precision medicine. The NCI plans to expand and scale the GDC with community engagement and additional funding.

Questions and Answers

Dr. Marcia R. Cruz-Correa, Associate Professor of Medicine and Biochemistry, University of Puerto Rico, and Basic and Translational Science Director, University of Puerto Rico Comprehensive Cancer Center, asked about the potential for matching mechanistic information with chemoprevention studies and whether minority groups will be targeted within the 1,000-case goal. Dr. Doroshow replied that successful functioning of the national network infrastructure first needs to be ensured and that case accrual from minority-based NCI Community Oncology Research Program (NCORP) sites is expected to be robust.

Dr. Kenneth C. Anderson, Kraft Family Professor of Medicine, Harvard Medical School, and Director, Lebow Institute for Myeloma Therapeutics, Dana-Farber Cancer Institute, inquired about the path forward for inclusion of hematologic malignancies. Dr. Doroshow responded that multiple myeloma foundations and others have expressed interest, but resources are needed.

Dr. Dang requested identification of the deliverables in the pipeline. Dr. Staudt explained that the GDC will be available for use in May 2016 and that 1,000 cell lines should exist within a 2-year period (100–200 cell lines currently are available).

Dr. Shannon asked about extending the use of organoids to robust *in vivo* models of more common cancers. He also recommended using FNLCR resources for banking and characterization needs, as well as for resource dissemination to the community. Dr. Staudt acknowledged the loss of some subclonal heterogeneity in organoids but added that aspects of tumor microenvironment can be addressed.

Dr. Basch inquired about the collection of data on PROs. Dr. Jeff Abrams, Acting Director, DCTD, replied that PROs add complexity to trials with small numbers of patients, but that follow-on trials would integrate PROs. Dr. Deborah Watkins Bruner, Robert W. Woodruff Chair of Nursing, Nell Hodgson Woodruff School of Nursing, and Associate Director for Outcomes Research, Winship Cancer Institute, Emory University, encouraged the NCI to incorporate common patient experiences, adherence, and cognitive function performance status into the data collection.

Dr. Walker asked about the use of a centralized model versus a distributed model. Dr. Staudt explained that initially a concerted effort is needed to develop expertise, but researchers who have developed cell lines already have inquired about opportunities to share them.

Dr. Lincoln D. Stein, Director, Informatics and BioComputing Platform, Ontario Institute for Cancer Research, asked whether NCI-MATCH will be quantifying targeted mutations and developing germline material. Dr. Doroshow responded that exome sequencing and RNA sequencing will be performed on all patients; germline studies will not be pursued initially, but appropriate material will be collected.

Ms. Smith commented on the need to effectively communicate with investigators about patient enrollment. Dr. Doroshow responded that patient enrollment has and will vary in each of the phases.

Dr. Eileen P. White, Distinguished Professor, Department of Molecular Biology and Biochemistry, and Associate Director for Basic Science, Rutgers Cancer Institute of New Jersey, commented on the immune system's role in cancer and asked about the potential for reconstituting mice with both the tumor and immune system, suggesting the use of genetically engineered mouse models. Dr. Staudt stated that some approaches are working, for example, a humanized mouse that has many of the cytokines that support hematopoiesis. Dr. Jacks added that the PMI initiatives being discussed do not describe all of the NCI's interests; other programs address other important models.

Dr. Olopade suggested ensuring that the 1,000 planned cell lines are representative of the diverse domestic and global populations. Dr. Staudt agreed, noting that accepting samples from community-based programs is dependent on the feasibility of shipping samples overnight.

Dr. Sangeeta N. Bhatia, John J. and Dorothy Wilson Professor, Division of Health Sciences and Technology and Electrical Engineering and Computer Science, Institute for Medical Engineering and Science, Koch Institute for Integrative Cancer Research, Broad Institute, Brigham and Women's Hospital, Massachusetts Institute of Technology, pointed out the need for combination toxicity testing for target engagement in normal tissues and shared with members that the Tissue Chip for Drug Screening Program, supported by the National Center for Advancing Translational Sciences (NCATS), is seeking drug recommendations. Dr. Staudt stated that one goal is to make available normal organoids that can be used in parallel to address toxicities.

Dr. Timothy J. Ley, Professor of Medicine and Genetics, Division of Oncology, Washington University School of Medicine, commented that large-scale patient databases could raise concerns about privacy. Dr. Kibbe acknowledged that some data cannot be made freely available and indicated that discussions about the topic continue.

IX. RFA/COOPERATIVE AGREEMENT CONCEPTS—NCI STAFF

Office of the Director

Non-Communicable Disease Regional Infrastructure Core Planning Grants (RFA)— Dr. Ted Trimble

Dr. Ted Trimble, Director, CGH, presented a concept to support activities for the planning and design of sustainable, regional research infrastructure cores (RICs) to address non-communicable diseases (NCDs) in low- and middle-income countries (LMICs) or regions. Dr. Trimble stated that LMICs are challenged in addressing NCDs, which share common risk factors—such as tobacco use, physical inactivity, unhealthy diet, harmful use of alcohol, and environmental factors—because of limited in-country support for research and training, inadequate research infrastructure, poor health care delivery services, lack of surveillance regard NCD management, and lack of coordination across relevant NCD activities. Members were told that many international studies conducted by organizations in the United States and the United Kingdom, including universities and Cancer Centers, operate in isolation. One notable exception is the Academic Model Providing Access to Healthcare (AMPATH), which provides a model partnership between Indiana University and Moi University in Kenya and a consortium of U.S. medical schools and other partners, including five NCI-designated Cancer Centers. The concept aims to establish partnerships similar to AMPATH, strengthen LMICs' commitment to public health research and implementation science, build an evidence base for NCD prevention and control, help build a global health career track for investigators focused on NCDs, and strengthen multidisciplinary research across NCDs.

Dr. Trimble said that this concept is for a planning phase that will be followed by two implementation phases. Activities of the planning grants include an assessment of NCD research needs and opportunities; encourage development of a consortium; development of a plan to coordinate research projects, infrastructure core development, and research training; and development of a strong application for core funding. An NCD RIC will include a partnership between a consortium of U.S. institutions and multiple LMIC institutions, the development of research core facilities, training and career development, and a focus on translating research into policy. Potential NIH partners include Fogarty International Center and other ICs to co-sponsor or make additional awards. Potential research areas span the cancer spectrum with a strong emphasis on implementation science and health disparities; core resources would

encompass effective grants and contracts management, research ethics oversight, bioinformatics and data management, health communications, and health economics and comparative effectiveness research. Evaluation criteria include the quality of the needs assessment, caliber of the research plan, a training plan, plans for the appropriate infrastructure cores, in-depth metrics, community engagement to identify the local research needs, strengthened administrative capacity of the LMIC institutions, and a credible plan for building a competitive research program. A network of NCD consortia is envisioned, as well as central NIH coordination led by the NCI.

Subcommittee Review. Dr. Basch expressed the Subcommittee's strong enthusiasm for the concept, which was seen as a reasonable initial step toward establishing a network, provided that the two follow-on phases are adequately resourced. The Subcommittee appreciated that global oncology is a rapidly evolving field, NCDs are recognized as essential to address in developing nations, and many existing relationships between U.S. Cancer Centers and other organizations can be leveraged. Concerns were expressed about the level of funding for this stage of the program, coordination with other Institutes to ensure that the NCI investment remains relevant to oncology, and incentives to sites that have until now been autonomous to coordinate their efforts. The Subcommittee emphasized the importance of developing a collaborative infrastructure early to ensure productive activities and also encouraged a 3-year funding cycle to allow time to overcome challenges from geographic and daily processes.

The first year cost is estimated at \$2 M for six P20 awards, with a total cost of \$4 M for 2 years.

Questions and Answers

Dr. Adamson suggested that operations be included as a core resource and wondered about the level of global coverage possible with six planning grants. Dr. Trimble clarified that applications can focus on any region in the world, and the consortia likely would address a limited number of countries where a U.S. commitment already exists. He confirmed that the consortia can extend between countries.

Dr. Adamson asked whether consortia will need to include NCDs beyond cancer to be competitive, since cancer specific consortia already exist. Dr. Trimble explained that the concept is focused on NCD research, and added that the NCI is working on separate efforts to strengthen cancer-specific research networks, such as a Burkitt's lymphoma network and a pediatric cancer network.

Motion. A motion to concur on the Center for Global Health's request for application (RFA) entitled "Non-Communicable Disease Regional Infrastructure Core Planning Grants" was approved unanimously.

Clinical Proteomic Tumor Analysis Consortium (CPTAC) (Reissue RFA/Coop. Agr.)— Dr. Henry Rodriguez

Subcommittee Review. Dr. Bhatia expressed the Subcommittee's support for the concept reissuance. Internal and external evaluations were favorable for reissuance, and the Subcommittee felt that the Program was productive in prior phases. The Subcommittee noted the Program's three major contributions: development and sharing of techniques, tools, and standardization for rigorous proteomics; proteomic analysis of several key tumor types; and establishment of a framework to integrate proteomic and genomic data. Future efforts will include analysis of additional tumor types, as well as application of the tools to explore clinically relevant phenomena (e.g., drug sensitivity and resistance), which the Subcommittee considered to be an important and timely direction. The Subcommittee recommended heightened awareness of the Program to maximize its impact.

NCI's Overview of Concept. Dr. Henry Rodriguez, Director, Center for Strategic Scientific Initiatives (CSSI), Office of Cancer Clinical Proteomics Research, informed members that CPTAC was

established to elucidate additional biology from deep proteomic analysis on genomically characterized tumors. A consortium of Proteome Characterization Centers (PCCs) coordinates standardized research activities and harmonizes analytical work flows and informatics to ensure high-quality data production and reproducibility. Through the U24 award, the PCCs provide data, assays, and reagents to the community. Members were informed that retrospectively collected biospecimens posed a major challenge in Year 1, because the effect of preanalytical variables, such as cold ischemia on protein measurement was unknown, and subsequently caused proteomic analysis to be postponed until the second year. Overall, CPTAC's investigations of colorectal, ovarian, and breast cancers have been successful and ongoing. The External Scientific Committee observed that the CPTAC structure has been successful and innovative at addressing proteomics cancer research and that CPTAC has accelerated the adoption of standardized proteomic approaches by the research community. It cautioned that innovative data analysis varied among PCCs and recommended avoiding retrospective samples, if possible.

Dr. Rodriguez explained to members that the reissuance concept has the following goals: (1) improve understanding of the proteogenomic complexity of tumors, with CPTAC's approach extending to five or six additional cancer types; and (2) apply CPTAC's analytically validated methodologies to clinical trials to address clinical and biological questions of drug response, toxicity prediction, and resistance. In addition to continuation of the PCCs for data generation, Proteogenomic Translational Research Centers (PTRCs) will conduct proteogenomic translation research on cancer models and clinical trial samples and Proteogenomic Data Analysis Centers (PGDACs) will develop innovative tools for data analysis across the entire proteome. It also will continue to provide resources to the community to accelerate proteomics science. He stated that the NCI has an opportunity to leverage its investments in cancer genomics by building on current achievements in cancer proteomics.

The first year cost is estimated at \$4 M for three U24 PCC awards, \$4.5 M for three U01 PTRC awards, and \$4.5M for four U01 PGDAC awards, with a total cost of \$20 M for PCCs, \$22.5 M for PTRCs, and \$22.5 M for PGDACs for 5 years.

Questions and Answers

Dr. Wicha suggested concentrating on single-cell analysis of individual tumors because a major barrier to treatment is tumor heterogeneity. Dr. Rodriguez responded that CPTAC has analyzed small sections of tumors using laser capture microdissection. Dr. Shannon suggested integrating diagnosis relapse tumor samples as well as diagnosis response tumor samples into the initiative.

Dr. Anderson asked about the potential for exploiting clinical annotation technology by collaborating with ongoing trials regarding precision medicine. Dr. Doroshow replied that relevant assays to ongoing NCI trials regarding precision medicine will be explored by CPTAC investigators.

Motion. A motion to concur on the Office of Cancer Clinical Proteomics Research's re-issuance request of RFA entitled "Clinical Proteomic Tumor Analysis Consortium (CPTAC)" was approved unanimously.

Genome Data Analysis Network (GDAN) (Reissue RFA/Coop. Agr.)—Dr. Louis M. Staudt

Subcommittee Review. Dr. Stein expressed the Subcommittee's support for the concept reissuance. He informed members that the GDAN is an extension of TCGA's Genome Data Analysis Centers (GDACs), which provided much of the computational backbone for TCGA. Collectively, GDACs have resulted in a large number of high-impact publications that encompass fundamental biological discoveries in the genomics of cancer, as well as a new generation of widely used algorithms. The Subcommittee felt that the RFA would benefit from enhanced discussion of (1) clinical correlation, (2) the integration of GDAN with precision medicine initiative and other large-scale genome-scale NCI

programs, and (3) community engagement in benchmarking and the selection of best current analysis tools.

NCI's Response to Subcommittee. (1) Dr. Staudt stated that integrating GDAN with clinical trials is critical to ensuring that new clinical correlations are found and validated in a statistically sound way. He agreed that clinical correlation should be highlighted as a core expertise. (2) Dr. Staudt stated that the GDAN will be involved in precision medicine as well as other CCG initiatives. A platform has been developed to process samples through the Biospecimen Core Repository, and a genome characterization contract is in place to generate primary data. Dr. Staudt lauded the TCGA as exemplary of team science and envisioned the GDAN as the core of the TCGA Analysis Working Groups that will be part of every project. (3) Dr. Staudt emphasized that community input is welcomed. The NCI Genomic Data Commons (GDC) will be the core database and knowledge base for all of GDAN's studies and will include both the raw data and the first level of analysis. An external advisory group and the Global Alliance for Genomics and Health (GA4GH) Data Working Group are engaged to help with choosing technologies, standards, and methods.

The first year cost is estimated at \$8.5 M for 14 U24 awards, with a total cost of \$45.5 M for 5 years.

Questions and Answers

Dr. Kevin P. White, James and Karen Frank Family Professor, Department of Human Genetics, Professor, Department of Ecology and Evolution, Director, Institute for Genomics and Systems Biology, Knapp Center for Biomedical Discovery, The University of Chicago, asked about a potential mechanism to ensure that specialized GDACs include community engagement. Dr. Staudt responded that bi-yearly TCGA meetings have included individuals from the GDC and plan to include representation from GDAN, individuals working in computational genomics, and others interested in genomics to help determine an agenda that would favor interaction between groups.

Motion. A motion to concur on the Office of the Director's (OD) re-issuance request of the RFA/Cooperative Agreement entitled "Genome Data Analysis Network (GDAN)" was approved unanimously.

X. U.S. NCI-CHINA RESEARCH COLLABORATIONS—DRS. TED TRIMBLE, LEE HELMAN, XIN WANG, ROBERT CROYLE, BRITT REID, STEPHEN J. CHANOCK, CHRISTIAN ABNET, BARRY KRAMER, YOU-LIN QIAO, AND YU WANG

Introduction. Dr. Trimble introduced a presentation on the U.S.-China partnership in cancer research, including the role of the CGH. The door between the United States and China was opened in 1971 with the meeting between Chairman Mao Zedong and President Richard Nixon. In 1979, Chairman Deng Xiaoping and President Jimmy Carter signed the U.S.-China Agreement on Cooperation in Science and Technology. The NCI Office of China Cancer Programs, dedicated to strengthening NCI's collaborations with China, was formed in 2008. China has much higher mortality rates from lung, stomach, liver, and esophageal cancer than the United States. Notably, Chinese women have remarkably high mortality from lung cancer, despite having low smoking rates. The NIH has jointly funded partnerships with the National Science Foundation of China (NSFC)—including projects with the National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health (NIMH), and National Institute of Neurological Disorders and Stroke (NINDS). The NIH also is collaborating with the Chinese Ministry of Science and Technology to explore opportunities for research, as well as to strengthen governance and peer review activities. With regard to training and capacity building, many Chinese postdoctoral fellows and researchers have visited and trained at the NCI, NCI-designated Cancer Centers, and universities.

Dr. Trimble introduced the presenters: Drs. Lee Helman, Scientific Director for Clinical Research, CCR, NCI; Xin Wei Wang, Deputy Chief, Laboratory of Human Carcinogenesis and Head, Liver Carcinogenesis Section, CCR; Robert Croyle, Director, DCCPS; Britt Reid, Deputy Associate Director, Epidemiology and Genomics Research Program, DCCPS, NCI; Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics (DCEG); Christian Abnet, Acting Chief, Nutritional Epidemiology Branch, DCEG, NCI; Barry Kramer, Director, Division of Cancer Prevention (DCP); You-Lin Qiao, Professor and Director, Department of Cancer Epidemiology, National Cancer Institute, Chinese Academy of Medical Sciences; and Yu Wang, Director-General, Chinese Center for Disease Control and Prevention.

Center for Cancer Research. Dr. Helman described connections with China at the CCR. Ten percent of CCR PIs are of Chinese descent. More than 150 recent alumni over the past 5 years are now working in China, primarily in academia (82%), but also in industry (11%). In 2014, 18 different PIs had active collaborations with 33 Chinese investigators at 28 different institutions, studying liver cancer, bladder cancer, neuroblastoma, and other cancers. The CCR has participated in and organized symposia in China, and the CCR is very involved with the U.S.-China Program for Biomedical Research Cooperation.

Dr. X. Wang stated that liver cancer is the second leading cause of cancer-related deaths worldwide, with the majority of new cases occurring in China, and has a very high mortality rate. Liver cancer is heterogeneous in its clinical presentation, demographics, environmental risk factors (e.g., HBV, HCV, chemical carcinogens), and lifestyle risk factors, which leads to highly heterogeneous tumor biology, both in genomics and the microenvironment. Collaborative studies of liver cancer between the NCI and Fudan University began in 1999. Pilot studies with Drs. Zhao-You Tang and Dr. Lun-Xiu Qin led to joint papers and the planning of larger studies, including a genome-wide association study (GWAS). A systems biology strategy to improve outcomes for liver cancer patients will involve developing a biobank and creating an information commons with omics-based classifications, leading to biomarker-guided interventions. Major accomplishments in research on liver cancer include proof-of-concept that the ability to metastasize may be an inherent quality of the primary tumor, which led to the development of the HeproDX test; a study showing the contribution of the tumor stroma to progression; the discovery of a gender-related biomarker, miR-26, which predicts response to interferon therapy; and the use of molecular and bioinformatics strategies to define liver cancer subtypes and drivers, which are potential targets. Collaborative studies between the NCI and Fudan University have been very productive, leading to more than 20 peer-reviewed publications, seven patents or patent applications, and multiple grants and awards. Challenges that remain include better defining tumor molecular subtypes; translating research findings to the clinic; evaluating less-studied risk factors (e.g., diet, lifestyle, liver fluke); addressing health disparities and global health; fostering bench/clinical/multi-institutional collaborations, such as the NCI-sponsored liver consortium; and addressing the limited funding and resources that are available for research and biobanks for a disease that is becoming more important in the United States.

Division of Cancer Control and Population Sciences. Dr. Croyle commented that the scientific opportunity represented by collaboration with China can be summed up as a greater range of exposure. DCCPS has four main research programs: epidemiology and genomics, surveillance, behavioral science, and health care delivery research, with epidemiology being the largest area of collaboration with China and an area in which increasing numbers of staff are working on issues of global health. Behavioral research and epidemiology and genomic research comprise the majority of the DCCPS grant portfolio, but health care delivery research is a growing funding area.

Dr. Reid reviewed some of the infrastructure and consortia collaborations between DCCPS and China. Mutual scientific interests include environmental exposures in cancer risk, genetic variance in

cancer risk, and tobacco control. DCCPS has a large and active portfolio of grants and cooperative agreements among Chinese populations with a variety of outcomes, including incidence of breast, colon, prostate, and other cancers. Critical cohorts include the Shanghai Women's Health Study (SWHS), Shanghai Men's Health Study, and Shanghai/Singapore Cohort. The SWHS was established in 1996 and has 75,000 participants with 5,000 incident cases; it has supported many junior investigators, it has resulted in more than 200 published manuscripts, and its resources have been used in more than 20 GWAS. SWHS investigators identified a new locus for breast cancer with relatively high frequency and a large effect size, and they established the Asia Colorectal Cancer Consortium, which showed a protective effect for soy-food intake against breast and colorectal cancer. Consortia with Chinese populations have been very successful in securing funding. The collaboration for tobacco control includes the China-U.S. Smokefree Workplace Partnership; mobile health (mHealth) projects that test mHealth tools, such as text messaging for smoking cessation; and support for the Health Information National Trends Survey (HINTS) in China. Top DCCPS scientific priorities for future collaborations include exploring health disparities in risk and occurrence, establishing Asian survivorship cohorts, and translating risk predictors into interventions.

Division of Cancer Epidemiology and Genetics. Dr. Chanock introduced an overview of DCEG studies in China, of which DCEG has more than 25 ongoing. DCEG has had more than 30 years of collaboration with China, including developing cancer maps that led to epidemiologic field studies and studying occupational exposures that were important in determining the carcinogenicity of chemicals. DCEG-Chinese collaborations are ongoing in many Chinese cities, and a large number of different academics have been trained and worked closely with DCEG. Special exposures studied in China have included occupational exposures to benzene, formaldehyde, trichloroethylene, and particulates, as well as the effects of physical activity. Observational studies, including studies of lung cancer in never-smoking women and people exposed to radon from living in underground dwellings, have the potential to lead to public health measures to decrease risk. The consortium to study the environmental and genetic etiology of lung cancer in never-smoking females has led to the identification of novel signals unique to non-smokers and linked residential histories to air pollution databases and satellite data. The ability to work closely with Chinese colleagues resulted in an individual exchange of data from GWAS of esophageal squamous carcinoma, the analysis of which led to the discovery of new susceptibility loci.

Dr. Abnet provided a review of DCEG studies in China of upper gastrointestinal (UGI) cancers. Eighty percent of the worldwide mortality from esophageal cancer is from squamous carcinomas, and half of those cancers occur in China. In 1985, a clinical trial of 30,000 Chinese farmers was sponsored by the NCI and NSFC to study UGI cancer. DCEG studies of UGI cancers in China include nutrition intervention trials for esophageal cancer, a *Helicobacter pylori* treatment trial for the prevention of gastric cancer, GWAS of esophageal and gastric cancer, and the effects of tooth loss and oral hygiene on the microbiome of the sputum and lung cancer risk. In the nutrition intervention trials, supplementation with a combination of vitamins and minerals, with selenium being the active agent, was found to reduce UGI risk, which had an incidence rate of approximately 20 percent. Early detection of esophageal lesions is key in successful intervention. Endoscopic localization with Lugol's solution was found to be highly specific for moderate and severe dysplasia, which has a high risk of conversion to tumors. A screening program was developed that was composed of identification of precursor lesions; endoscopic localization; staging; and therapy, for which many options exist. Long-term followup of endoscopic screening showed that early detection and intervention resulted in a significant reduction in esophageal squamous-cell carcinoma mortality. Non-endoscopic screening methods are needed, however, and methylation arrays and chromosomal abnormalities have been shown to be predictive in biorepository samples.

Division of Cancer Prevention. Dr. Kramer surveyed three primary collaborations between DCP and China: the Cancer Screening Trial Feasibility Study, the China Early Detection Research Network (EDRN), and Chinese translation of the Physician Data Query (PDQ[®]) database. Primary collaborators

include the National Institute/Hospital of Chinese Academy of Medical Sciences (CICAMS) and National Cancer Center (NCC), as well as the NCI Office of Communications and Public Liaison for the Chinese translation of the PDQ database. For the China Cancer Screening Trial Feasibility Study, CICAMS was very interested in lung and colorectal cancer screening, including confirming the National Lung Screening Trial (NLST) in a Chinese urban population, particularly with regard to generalizability and because of a different spectrum of causative exposures. The design of the feasibility study was to recruit from three cities in China of high, middle, and low socioeconomic status and have three study arms. A memorandum of understanding for the study was signed in May 2013, and the study now has completed the baseline screening phase. Center recruitment has been completed, although a significantly lower proportion of eligible participants were randomized in the lower socioeconomic status city. Preliminary data show a wide variation in computerized tomography (CT) lung abnormality by screening center and a wide range in the rate of non-calcified nodules/masses detected. Regarding the China EDRN, CICAMS is interested in establishing an EDRN infrastructure. To this end, joint monthly U.S.-China conference calls have been held, a common informatics center is assisting in establishing China databases, and China has sent a visiting scientist to the NCI to learn about EDRN processes and studies. The Chinese translation of the PDQ database is intended to extend the reach of PDQ cancer information to Chinese-speaking health professionals. In its pilot phase, health professional summaries for six cancer types of highest public health interest in China have been translated, reviewed by content experts, and placed online as the initial effort toward constructing the full website.

Impact of NCI Research Collaboration From China's Perspective. Dr. Qiao informed members about the importance of the collaboration between the U.S. NCI and the China Center for Disease Control and Prevention (China CDC). China first began a collaboration with the NCI in 1982 with etiological case-control studies on esophageal, lung, stomach, and choriocarcinoma cancers. Following these studies were a collaboration on a nutrition intervention trial, on which followup has continued for more than 30 years, and many etiological studies. Other notable collaborations have included cytology and HPV DNA tests for cervical cancer and an endoscopy screening collaboration, which included a visit to China by then-President Bill Clinton. Because of the discomfort caused by balloon cytology, China, with assistance from the United States, developed an endoscopy screening method, which also was able to include people living in the countryside. Dr. Qiao also noted several NCI–China educational and training programs. The Cancer Prevention Academic Course, organized since 1986, has benefitted many young Chinese investigators, including Dr. Qiao himself. Others include the NIH Fogarty International Clinical Research Scholars and Fellows Program, the Fulbright Public Health Program, and Fogarty Global Health Fellows.

Collaboration between the U.S. NCI and China CDC has had a strong positive impact on the Chinese. In Linxian, China, where the early esophageal and lung cancer studies took place, a public health plan put forth by Chinese investigators has led to an increase in healthy nutrition and a reduction in mortality from common cancers and elderly diseases. Data from a long-term study in a community in which one-time endoscopic screenings were given has revealed a 29 percent decrease in cumulative incidence of esophageal cancer among the target population and a 34 percent reduction in cumulative mortality from esophageal cancer. Dr. Qiao explained that collaborating with the NCI also has taught the Chinese about procedures surrounding ethical issues. For example, China has modeled its Institutional Review Boards on NCI projects. He also recognized the NCI's impact on Chinese health policy and regulatory concerns. Roundtable discussions have been held on such issues as HPV vaccine implementation and comprehensive prevention of cervical cancer in China. Dr. Qiao shared that in 2012, China's hospital director signed an agreement with Dr. Harold Varmus, then-Director of the NCI, to ensure future U.S. NCI–China CDC collaborations. Efforts will include the National Cervical Cancer Prevention Plan and Strategies, the Need for National Commitments to Cancer Research to Guide Public Health Investment and Practice, and the NCI Summer Curriculum in Cancer Prevention in China.

Dr. Y. Wang provided additional context for the NCI–China CDC collaboration, explaining that nearly 24 percent of deaths in China are caused by cancer, with especially high levels of lung, liver, and stomach cancers. The World Health Organization recommends tobacco control, physical exercise, and healthy nutrition to assist with cancer prevention, and China has taken steps in these directions. China also has engaged in a cancer screening project and increased its use of vaccines for cancer prevention. For example, an increase in hepatitis B vaccinations has reduced the incidence of liver cancer. Members were informed of a collaborative study begun with the NCI several decades ago on the occupational hazard benzene. The study helped researchers understand the biomarkers associated with benzene exposure and the biological effects at low exposure levels. The study also formed the basis of changing occupational threshold limits in China and has been used by the U.S. Environmental Protection Agency to reconsider its basis for allowable environmental levels.

Dr. Y. Wang elaborated on the long-term Chinese Children and Families Cohort Study (CFCS), a collaboration that began in 1993 as the Community Intervention Program of Folic Acid Supplements for Neural Tube Defect Prevention. The Program, which studied 240,000 pairs of mothers and offspring, showed that the prevalence of neural tube birth defects was reduced significantly when mothers were given folic acid supplements periconceptionally. This study informed the policy of folic acid supplements in China. Recently three pilot studies, including two related to cancers, were completed on a fraction of the CFCS families, and in progress is a feasibility study to determine whether CFCS families can be re-identified on a substantially larger scale.

Dr. Y. Wang expressed appreciation to the NCI for its ongoing collaboration with China on cancer research. He stated that areas for future collaboration include expanding research on the association of early life exposures and chronic diseases, such as cancer; strengthening cooperation, communication, and training on data collection and management, as well as on analysis of descriptive and analytic studies between the United States and China; continuing expansion and cooperation in the field on the study of cancer risk factors; and enhancing research and collaboration on cancer prevention, intervention, and vaccine development and application.

Discussion. Dr. Olopade thanked the CGH for providing focused information on cancer research efforts in China to the NCAB Subcommittee on Global Cancer Research and asked about similarities between patterns of cancer found in China and those of Asian immigrants living in the United States. Dr. Wang pointed out that an emphasis on tumor subtypes allows a more global comparison of commonalities or uniqueness. He added that because of significant heterogeneity in genomic and phenotypic levels, both functional and genomic studies are needed to determine targetable drivers and advance precision medicine.

Dr. Ley queried about the NCI's total investment supporting collaborative research in China, the percentage allocated to intramural versus extramural studies, and other NIH collaborative activities with China. Dr. Kramer responded that partnerships and country visits between the DCP and China focus on the PDQ[®] database and screening centers. Dr. Trimble indicated that NIAID; the National Heart, Lung, and Blood Institute (NHLBI); and the *Eunice Kennedy Shriver* National Institute for Child Health and Human Development (NICHD) have collaborations with China. Dr. Qiao described one form of collaboration with American medical students in China receiving support for living expenses from a U.S. organization, such as Fogarty, and utilizing Chinese training facilities.

Dr. Marcia R. Cruz-Correa asked whether a past RFA on investment for low technology received applications regarding endoscopic screening. Dr. Trimble responded that no fundable applications for esophageal cancer were received in the first round of funding, but a project concerning the early diagnosis of hepatitis C infection was funded.

XI. ADJOURNMENT—DR. TYLER E. JACKS

There being no further business, the 5th joint meeting of the BSA/NCAB was adjourned at 4:30 p.m. on Wednesday, 24 June 2015.

XII. NCAB CLOSED SESSION—DR. TYLER E. JACKS

This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c)(4), 552b(c)(6), Title 5 U.S. code, and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).

*The NCAB **en bloc** vote for concurrence with IRG recommendations was unanimous. During the closed session, a total of 2,769 NCI applications requesting direct cost support of \$915,636,681 and 14 FDA applications were reviewed.*

XIII. ADJOURNMENT—DR. TYLER E. JACKS

There being no further business, the Closed Session meeting of the NCAB was adjourned at 5:30 p.m. on Wednesday, 24 June 2015.

Date

Tyler E. Jacks, M.D., Chair, NCAB

Date

Paulette S. Gray, Ph.D., Executive Secretary

Report from the Acting Director

*Douglas R. Lowy
Acting Director, National Cancer Institute,
National Institutes of Health*

Outstanding Investigator Award

- To provide long-term support to experienced investigators with outstanding records of cancer research productivity who propose to conduct exceptional research.
- To allow investigators the opportunity to take greater risks, be more adventurous in their lines of inquiry, or take the time to develop new techniques

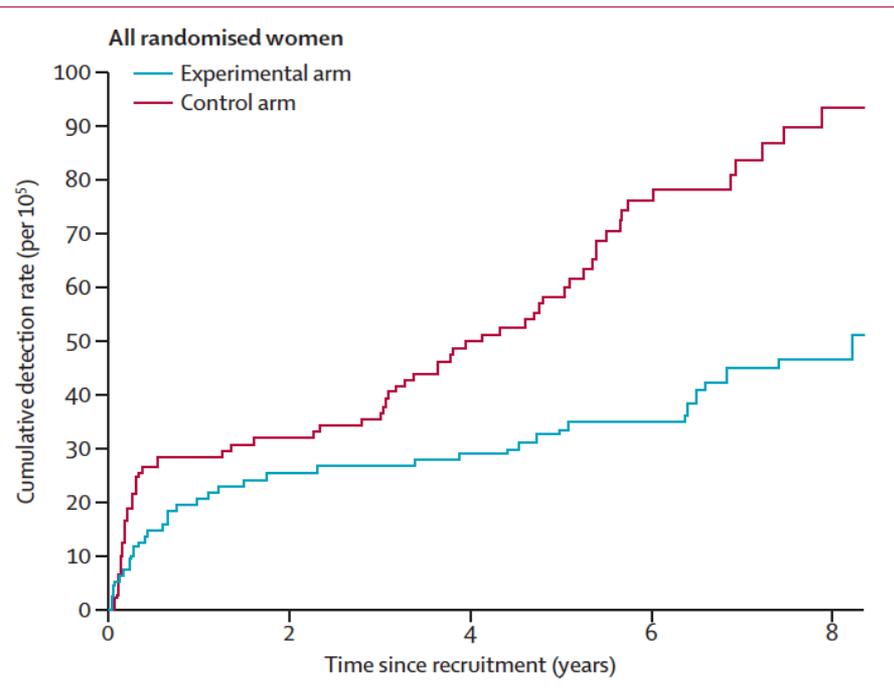
Precision Medicine in Cancer Treatment

- President Obama has proposed \$70 million in his FY16 budget for the Precision Medicine Initiative in Oncology (PMI-Oncology)
- Future workshop to explore the translational potential for the specific re-activation and/or replacement of tumor suppressor gene activities

Precision Medicine in **Cancer Screening**

- Moving from screening based mainly on “pattern recognition” towards screening based mainly on molecular understanding of disease and its application to molecular diagnostics
- The example of **cervical cancer screening**
- Cytologic (Pap) screening is more sensitive for detecting squamous cell cancer precursors than adenocarcinoma precursors; squamous cell cancer incidence has decreased, but not adenocarcinoma

HPV testing can prevent more cervical cancers, especially adenocarcinomas, than cytology



	Pooled rate ratio* (95% CI)
Morphology	
Squamous-cell carcinoma	0.78 (0.49–1.25)
Adenocarcinoma	0.31 (0.14–0.69)
Adenocarcinoma vs squamous-cell carcinoma	0.34 (0.12–0.90)

* Ratio of incidence with HPV testing vs. incidence with cytology

Pooled cervical cancer incidence from 4 randomized controlled trials of **cytology (control arm)** vs. **HPV testing (experimental arm)**

Precision Medicine in **Cancer Prevention**

- The example of **aspirin**
- Aspirin can reduce the risk of several cancers, especially colorectal cancer
- Concern about side effects from aspirin (especially an increased risk of bleeding) has prevented aspirin from being recommended for reducing cancer risk
- To increase the benefit/harm ratio, use molecular understanding to risk-stratify those patients who will derive the most benefit

High 15-Hydroxyprostaglandin (15-HPGD) in normal colon is associated with reduced risk of CRC in regular aspirin users

	Non-Users	Regular aspirin users
All CRC	1.0	0.73 (0.62-0.86)
High 15-PGDH CRC	1.0	0.49 (0.34-0.71)
Low 15-PGDH CRC	1.0	0.90 (0.63-1.27)

Background information: 15-HPGD is down-regulated in CRC; 15-HPGD knock-out mice have increased colon tumors that are resistant to COX-2 inhibitors

Focus on specific cancers with health disparities (high-risk populations)

- Identify the specific cancers
- Some possible examples: colorectal cancer, liver cancer, breast cancer, prostate cancer
- Identify the risk factors and their relative contribution to the disparities: biologic factors, life-style factors, health care access/utilization
- Explore efforts to mitigate the risk factors

Novel recurrently mutated genes in African American colon cancers

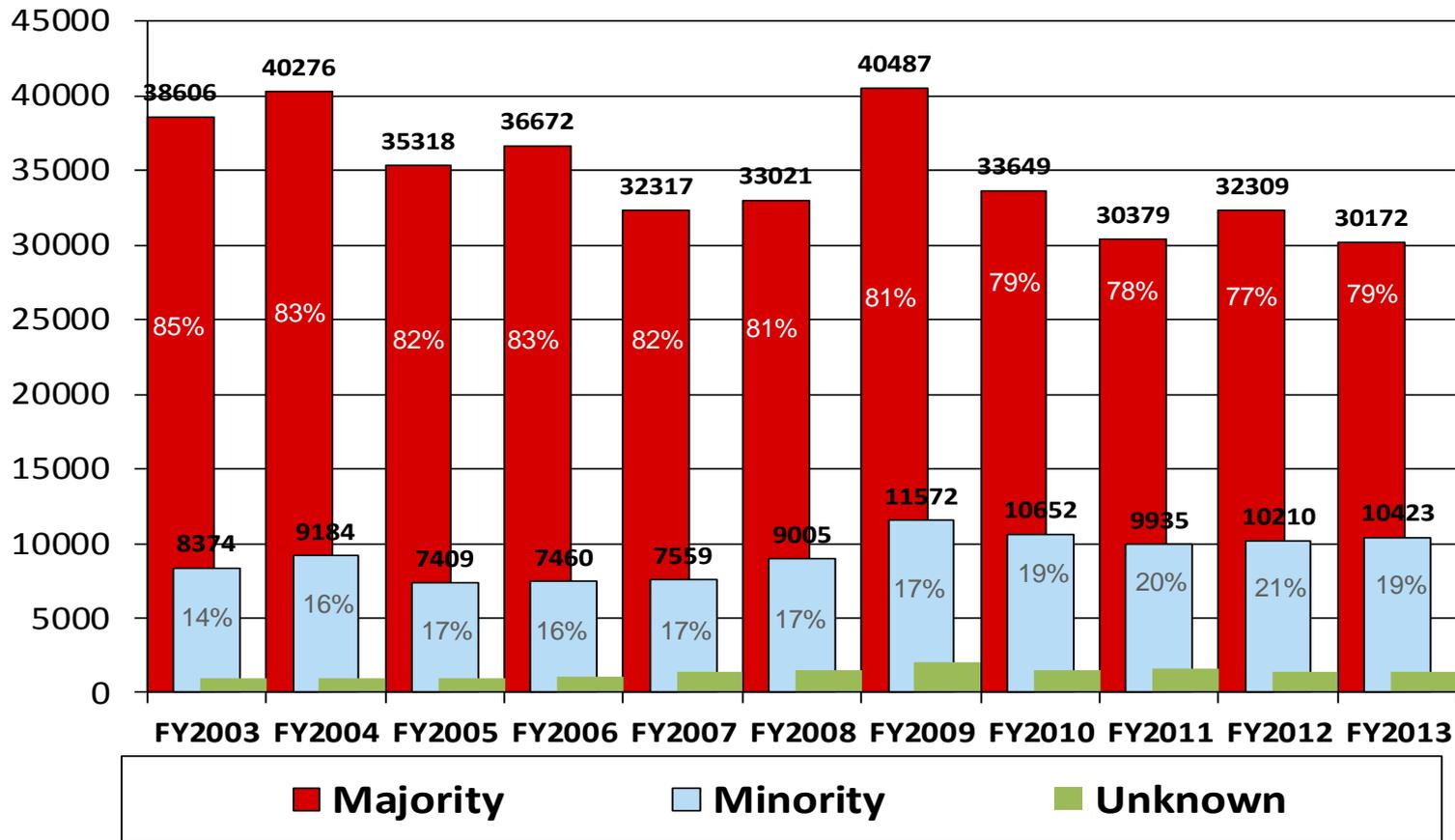
Kishore Guda^{a,b,c}, Martina L. Veigl^{b,c,1}, Vinay Varadan^{a,b,1}, Arman Nosrati^d, Lakshmeswari Ravi^d, James Lutterbaugh^d, Lydia Beard^d, James K. V. Willson^e, W. David Sedwick^{b,c,d}, Zhenghe John Wang^{b,f}, Neil Molyneaux^f, Alexander Miron^f, Mark D. Adams^g, Robert C. Elston^{b,h}, Sanford D. Markowitz^{b,c,d,i,2,3}, and Joseph E. Willis^{b,c,i,j,2}

^cDepartment of Medicine, ^fDepartment of Genetics and Genome Sciences, ^hDepartment of Epidemiology and Biostatistics, ^jDepartment of Pathology, ^aDivision of General Medical Sciences-Oncology, ^dDivision of Hematology and Oncology, ^bCase Comprehensive Cancer Center, and ⁱCase Medical Center, Case Western Reserve University, Cleveland, OH 44106; ^eHarold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, TX 75390; and ^gJ. Craig Venter Institute, La Jolla, CA 92037

“...Mutations in a set of 15...genes appear to be strongly preferentially associated with CRCs arising in AA versus Caucasian individuals, suggesting an important difference in the mutational landscapes of CRCs arising in different ethnic groups. “

Guda et al., 2015. Proc. Natl. Acad. Sci. 112:1149

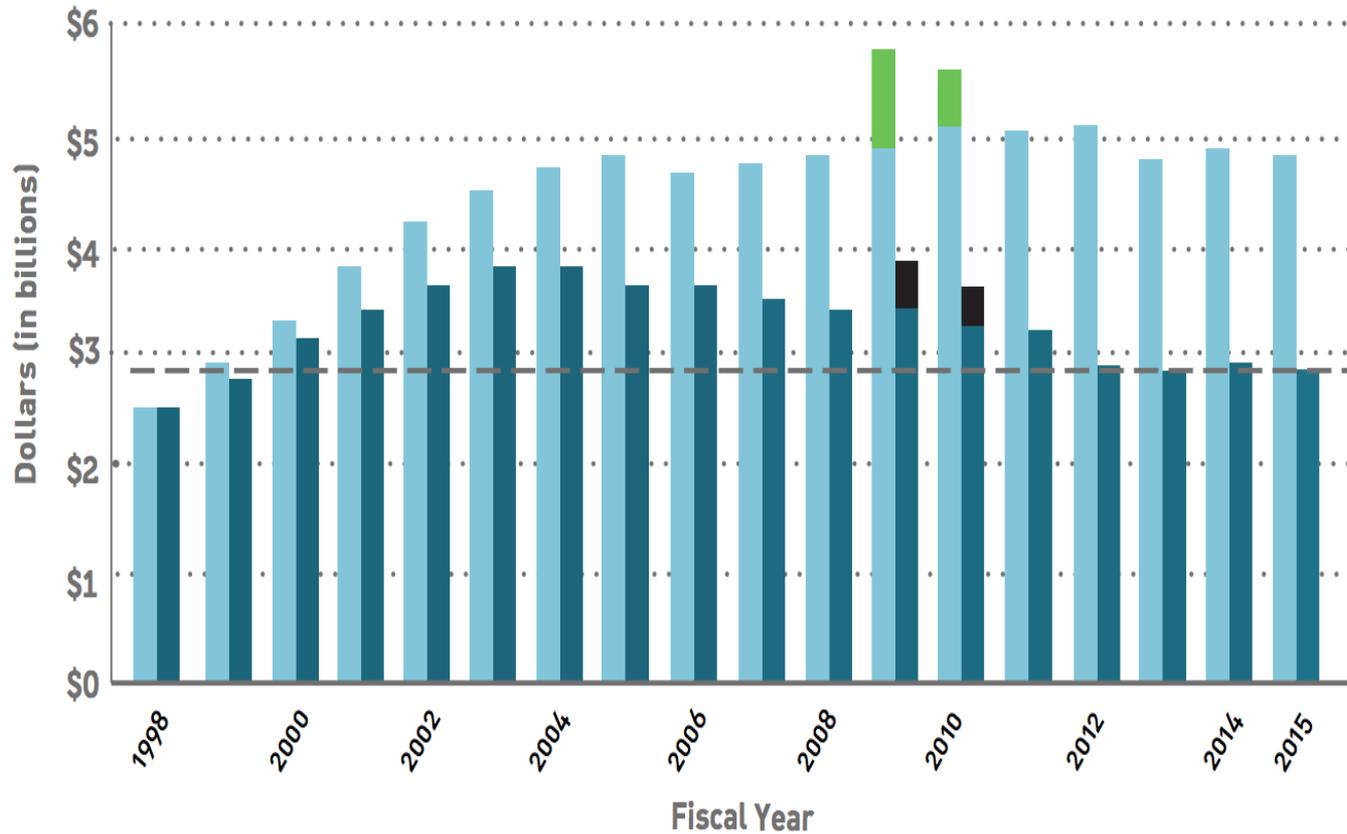
Minority Enrollment to NCI Cooperative Group Clinical Trials



Worta McKaskill-Stevens et al, NCI Community Oncology Research Program, unpublished data

Strong Support for Basic Research

The Declining Purchasing Power of the NCI Budget



■ NCI Budget
 ■ NCI Budget Adjusted for Inflation (FY 1998 dollars)
 ■ ARRA Funding (Public Law 111-5)
 ■ ARRA in 1998 Dollars

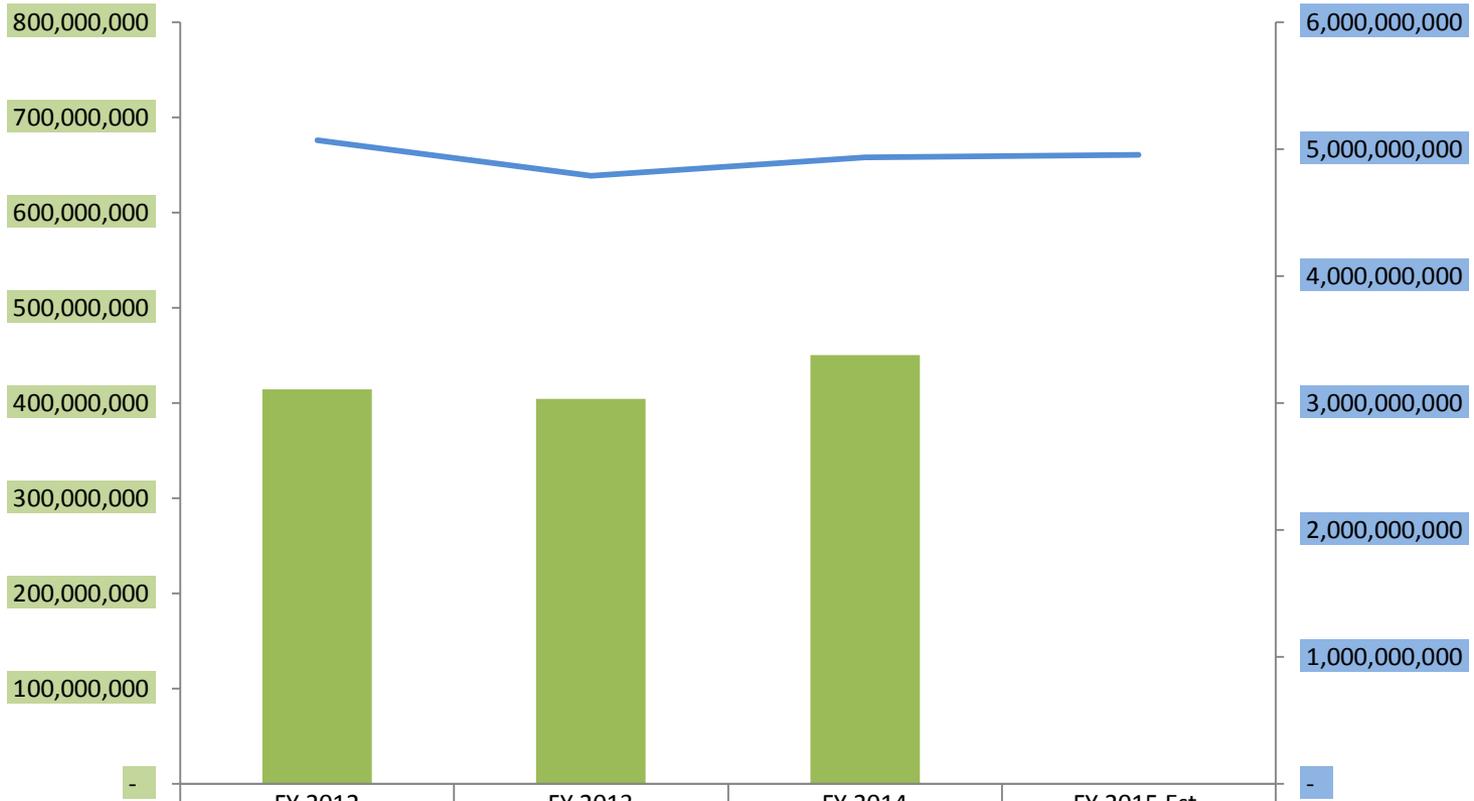
-- The dashed line at \$2.9 billion shows that the current NCI budget, adjusted for inflation, is essentially the same as the NCI budget in FY 1999.

Source: NCI Office of Budget and Finance

Competing RPG & NCI Total Obligations

Competing RPG Obligations

NCI Total Obligations



	FY 2012	FY 2013	FY 2014	FY 2015 Est.
Competing RPGs - Obligations	414,003,721	403,944,814	450,476,095	-
Competing RPGs - Count	1,085	1,095	1,207	-
NCI Total Obligations	5,067,341,795	4,789,014,389	4,932,368,225	4,953,028,000

■ Competing RPGs - Obligations
 — NCI Total Obligations

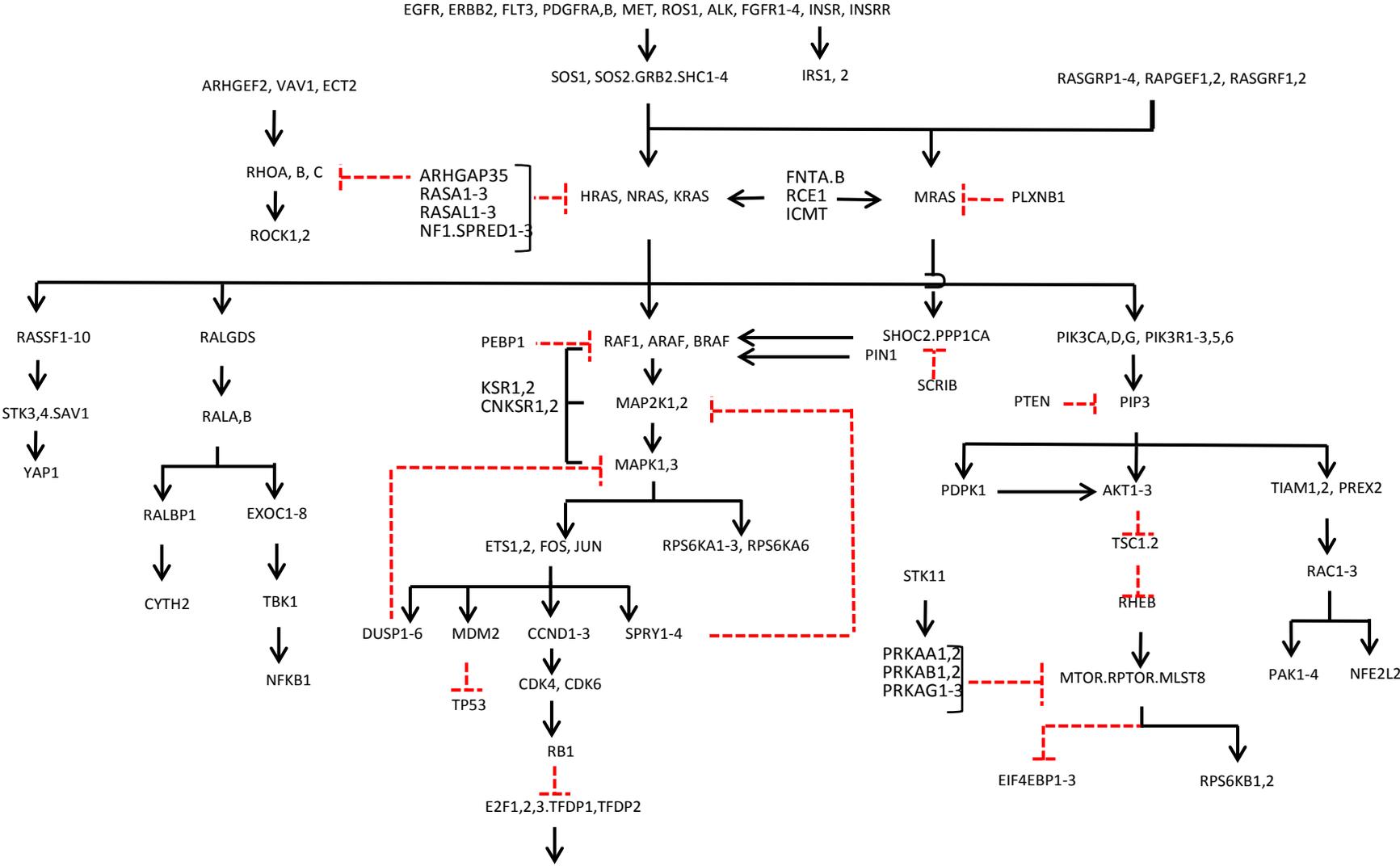
Recent modifications to RPG pool

- Decreasing the cuts to modular grants from 17% to 8.5%.
- Outstanding Investigator Awards: will increase the average size of the awards

NCI Cancer Centers

- P30 core grants

Ras pathway v2.0



Ras pathway clones

- **2 sequence-validated Gateway Entry clones for each gene (for generating N or C terminal fusions)**
- **180 total genes**
 - 17 not available commercially in the most biologically relevant isoform
 - 32 additionally not available without non-silent mutations
- **350 of 360 clones completed by July 17th**
- **Clones available through Dom Esposito: espositod@mail.nih.gov**

FNLCR Recompete

- NCI has begun the recompetition of the Operations and Technical Support (OTS) contract that runs NCI's Federally Funded Research and Development Center (FFRDC)
- Leidos Biomedical Research, Inc. currently administers the contract
- Information concerning the competitive process will be announced on [FedBizOpps](#) as well as at the [FNLCR Acquisition Portal](#)
- Pre-Proposal Conference Oct. 1 – 2, 2015
- Please help spread the word – we are doing our utmost to ensure a fair and open contract competition

Recent Personnel Changes

Retirements

- Bob Wiltrout, Center for Cancer Research (CCR)
- Joe Tomaszewski, Division of Cancer Treatment and Diagnosis (DCTD)
- Susan Erickson, Office of Government and Congressional Relations (OGCR)

New Leadership

- Toby Hecht, Deputy Director, DCTD
- Lee Helman, Acting Director, CCR
- Glenn Merlino, Acting Scientific Director (Basic), CCR
- MK Holohan, Acting Director, OGCR
- Peter Garrett, Director, Office of Communications and Public Liaison (OCPL)

Center for Global Health

- Marie Ricciardone, Ph.D.

New Version of Cancer.gov and Cancer.gov/espanol



NCI Office of Communications and Public Liaison, especially Peter Garrett and Lakshmi Grama



NCI-MATCH Targeted Treatment
Clinical Trial Launches at ASCO

LaRed21

Instituto Nacional del Cáncer en
EE.UU. en el mayor ensayo genético
hasta ahora trata mutaciones
específicas en tumores

The Washington Post

Health & Science

Cancer trials are changing. That could mean
faster access to better drugs.

OneLive

Largest-Ever Precision Medicine
Oncology Trial Ready for Launch

THE WALL STREET JOURNAL.

U.S. Cancer Study to Match Existing Drugs to Genetic Mutations

Study marks ambitious effort to advance emerging field of precision medicine

THE CANCER LETTER

NCI-MATCH to Bring in Public, Private Funds,
Giving NCI New Urgent Scientific Agenda

By Paul Goldberg

C-SPAN



AP THE BIG STORY

Novel government cancer study will test precision
medicine

By MARILYN MARCHIONE Jun. 1, 2015 11:56 AM EDT

abc NEWS

Chicago Tribune

U.S. News

The Washington Post

To Your Health

A new way to study cancer and its
treatments

Pittsburgh Post-Gazette®

Genetic tailoring? Pittsburgh-area hospitals set
to join nationwide cancer trial

June 3, 2015 2:22 PM

Los Angeles Times

Cancer trials aim to shore up
'precision medicine's' base of
evidence

Shanghai Daily

上海日报

U.S. announces schedule of trial for linking
targeted cancer drugs to gene mutations

Jun 02, 2015

REUTERS

Health | Mon Jun 1, 2015 5:43pm EDT

Large U.S. cancer trial to match genetic glitches to
targeted drugs

CHICAGO | BY JULIE STEEN-HUYSEN



**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol

Barbara K. Rimer, DrPH
Chair, President's Cancer Panel



Update for the National Cancer Advisory Board

June 24, 2015



Mission

The Panel shall monitor the development and execution of the activities of the National Cancer Program, and shall report directly to the President.

Any delays or blockages in the rapid execution of the Program shall immediately be brought to the attention of the President.

Authority: 42 U.S.C. 285a-4; Sec. 415 of the Public Health Service Act, as amended



Members

Barbara K. Rimer, DrPH

Univ. of North Carolina at Chapel Hill

Hill Harper, JD

Cancer Survivor, Actor, and Best-Selling Author



Owen N. Witte, MD

University of California Los Angeles





Overview

2012-2013 Report to the President

UPDATE: *Accelerating HPV Vaccine Uptake:
Urgency for Action to Prevent Cancer*

2014-2015 Series

*Connected Health: Improving Patients'
Engagement and Activation for Cancer-Related
Health Outcomes*



2012-2013 Report to the President – IMPACT

Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer



HPV Vaccines **Prevent Cancers**.
Why Are **So Few** U.S. Adolescents Vaccinated?



A Report to the President of the United States
from
The President's Cancer Panel

President's Cancer Panel Annual Report 2012-2013

ACCELERATING HPV VACCINE UPTAKE: URGENCY FOR ACTION TO PREVENT CANCER

Share:

Human papillomaviruses (HPV) cause most cases of cervical cancer and large proportions of vaginal, vulvar, anal, penile, and oropharyngeal cancers. HPV also causes genital warts and recurrent respiratory papillomatosis. HPV vaccines could dramatically reduce the incidence of HPV-associated cancers and other conditions among both females and males, but uptake of the vaccines has fallen short of target levels. The President's Cancer Panel finds underuse of HPV vaccines a serious but correctable threat to progress against cancer. In this report, the Panel presents four goals to increase HPV vaccine uptake: three of these focus on the United States and the fourth addresses ways the United States can help to increase global uptake of the vaccines. Several high-priority research questions related to HPV and HPV vaccines also are identified.

- Letter to President Obama
- Executive Summary
- Recommendations at a Glance
- Download Full Report (PDF)

Click below to read more.

HOW TO ACCELERATE HPV VACCINE UPTAKE IN THE U.S.



➤ Reduce Missed Clinical Opportunities to Recommend and Administer Vaccines



➤ Increase Parents', Caregivers', and Adolescents' Acceptance of HPV Vaccines



➤ Maximize Access to HPV Vaccination Services

INCREASE GLOBAL HPV VACCINATION

CONDUCT HIGH-PRIORITY RESEARCH



National HPV Vaccination Roundtable (Feb. 2015)

- ❑ With support from the ACS and CDC, a national coalition of public, private, and voluntary organizations is collaborating to increase HPV vaccination coverage.

- ❑ First meeting held Feb. 23-24, 2015, in Atlanta:
 - *Meeting goal: identify and define pilot projects for Roundtable implementation.*
 - **Pilot projects must be responsive to the PCP's HPV report recommendations.**



National Vaccine Advisory Committee (June 2015)

On June 9, 2015, NVAC voted to approve the 5 recommendations of the NVAC HPV Working Group:

- 1. Endorse the PCP report and adopt the recommendations therein.***
- 2. Endorse monitoring “the status of uptake and implementation of PCP recommendations” through an annual progress report from HPV immunization stakeholders.***

*Adopted June 2014



National Vaccine Advisory Committee (June 2015)

3. ASH* should work with relevant agencies and stakeholders to develop evidence-based, effective, coordinated communications strategies to **increase clinician recommendations** for HPV vaccination to adolescents.
4. ASH should work with stakeholders to strengthen the immunization system in order to **maximize access** to adolescent vaccinations, including HPV vaccines.

* Assistant Secretary for Health



National Vaccine Advisory Committee (June 2015)

5. ASH should encourage the review or development of available data that could lead to a **simplified HPV vaccination schedule.**



Research on the HPV Vaccine: Update from NCI

□ Intramural

- Proposed trial on single dose (direct evaluation of 2- and 1-dose regimens) is **responsive to PCP recommendation to safely reduce number of doses.**

□ Extramural

- Cancer Center grant supplements were awarded to gather local data on vaccine uptake, barriers, needs, and collaborators.
- New extramural announcements (in process) address **PCP's call for research on communication about HPV vaccines.**



Upcoming HPV Report Presentations

INNOVATIONS In Cancer Prevention and Research Conference

November 9-10, 2015 • Renaissance Arboretum Hotel in Austin

Abby Sandler, PhD, will give keynote address on PCP's HPV report at the Cancer Prevention & Research Institute of Texas' November conference.



2014-2015 Series

Connected Health: Improving Patients' Engagement and Activation for Cancer-Related Health Outcomes



Improve communication, health care, health & reduce costs

“The participation of patients in their own healthcare could substantially improve their care...Access to electronic personal health information and interfaces that make it easy for public and private clinical organizations to share health information with each other and with patients could enable healthcare providers and patients to collaborate in informed decision-making.”

P. 17, PCAST, Realizing Potential of Health IT, 2010



Series Overview

Identifying the Opportunity

- Planning meeting San Diego, 6/2014
Cancer Communication in the Digital Era: Opportunities & Challenges
- 1st focused workshop held in Boston, 12/2014
Engaging Patients with Connected Health Technologies
- 2nd focused workshop San Francisco, 3/2015
The Personal Health Data Revolution, Connected Health, and Cancer



Series Overview (cont.)

Vision and Recommendations for the Future

- ❑ Next meeting: Chicago, 7/9/2015.
- ❑ Objective **1**: Review and develop agreement on a reasonably attainable future state.
- ❑ Objective **2**: Identify concrete recommendations for achieving future state for the benefit of patients and the public.



Workshop 1: Engaging Patients with Connected Health Technologies

*Cambridge, MA
December 11, 2014*



- ❑ Connected healthcare led to **50%** drop in general readmissions, **69%** drop in BP. (Kvedar)
- ❑ Wrist-worn devices showed **94%** rate for accurate prediction of convulsive seizures. (Piccard)
- ❑ Connected infrastructures are needed for team care. (Mandl)
- ❑ Precision medicine requires integration of research, care, and data. (Kibbe)
- ❑ Improving access is critical to eliminate disparities. (Gibbons)





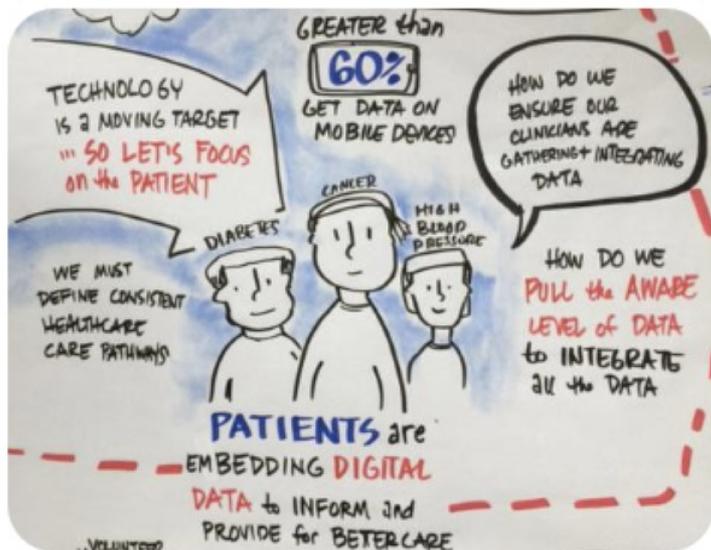
Workshop 2: The Personal Health Data Revolution, Connected Health, & Cancer

*San Francisco, CA
March 26, 2015*



The Personal Health Data Revolution,
Connected Health, and Cancer

March 26, 2015 • San Francisco, CA
Hyatt Regency San Francisco
[#cHealth4Cancer](#)



- ❑ Open data, patient wisdom and public involvement in research (Friend)
- ❑ Patient-centered, data-driven, coordinated, & continuous (Middleton)
- ❑ The Internet of things & mobile leave digital traces of everyday life. (Patrick)
- ❑ Use connected data to improve quality and support decisions in oncology. (Schilsky)
- ❑ Connected care in cancer: 6 X Pap, 6 X Mam, 10 X CRC & 100% equity (Shah)



Workshop 3: The Connected Cancer Patient: Vision for the Future & Recommendations for Action

*Chicago, IL
July 9, 2015*



**The Connected Cancer Patient:
Vision for the Future and
Recommendations for Action**

July 9, 2015 • 8:30 am to 5:00 pm
W Chicago Lakeshore Hotel
#cHealth4Cancer



Participants will contemplate and respond to a scenario for a **future connected health system by the year 2020** and consider key areas for potential intervention:

- ❑ Personal health information and data sharing
- ❑ Person- and family-centered care
- ❑ Optimal use of devices, sensors, and apps
- ❑ National health information infrastructure



Fractures in Cancer Care



Primary Prevention:

e.g., “**70%** of smokers visit healthcare, but few receive adequate follow-up.” Fiore (2013)

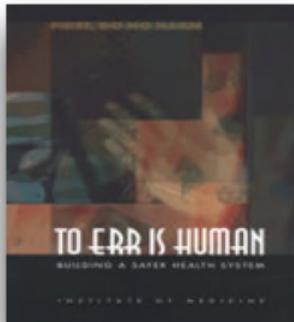
Survivorship

Communication problems have devastating consequences for cancer survivors. (IOM, 2005)



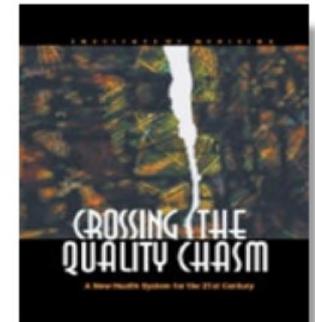
Secondary Prevention:

e.g., 56% of late stage cervical cancer cases in community hospital had not been screened. (Zapka et al, 2010)



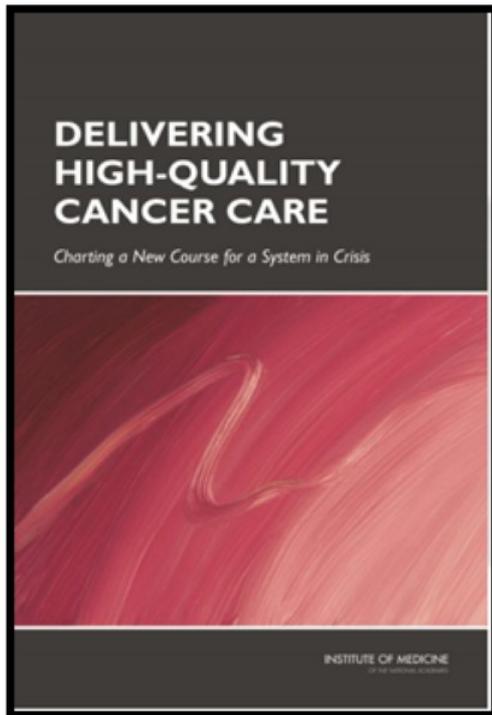
Treatment Adherence:

e.g., “**63%** of teens & young adults do not adhere to cancer Rx regimens,” Kondryn et al. (*Lancet Onc*, 2011)





Stresses in Oncology



<http://www.iom.edu/Reports/2013/Delivering-High-Quality-Cancer-Care-Charting-a-New-Course-for-a-System-in-Crisis.aspx>

Stresses that will likely exacerbate fractures, obstruct progress:

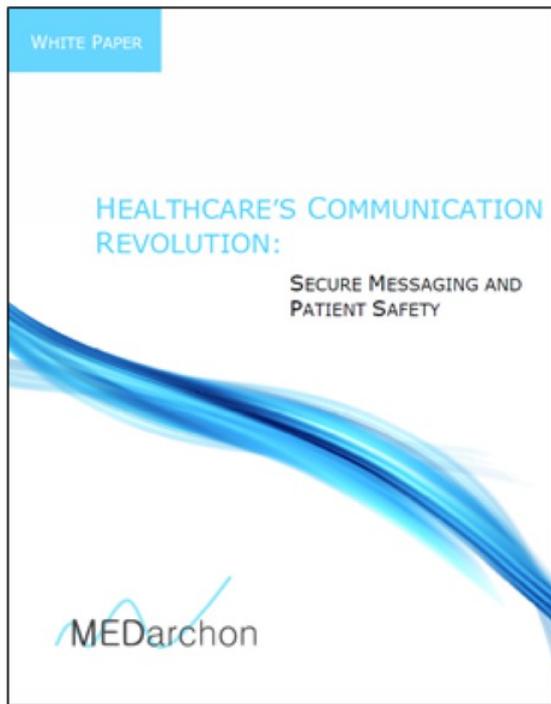
- ❑ Aging demographics
- ❑ Increasing incidence overall
- ❑ Complexity in oncology care
- ❑ Increasing number of survivors (18 million by 2022)
- ❑ Shrinking work force
- ❑ Rise in treatment costs



The Healthcare Communication Revolution: Bridging Disconnects



I. Make Effective Communications An Organizational Priority to Protect the Safety of Patients



- ❑ Fix patient handoffs (50% of errors).
- ❑ Provide asynchronous channels (to ensure reliable communication).
- ❑ Use smart scheduling, issue routing (as preemptive error control).
- ❑ Offer secure messaging (to preserve privacy and confidentiality).
- ❑ Leverage eHealth, telemedicine apps (to move care to patient).



Unleashing the "Power of Connectivity"* in Oncology



UNLEASHING THE POWER OF CONNECTIVITY IN HEALTH CARE.

A health care crisis of communication.

Over the last 50 years medical science has advanced exponentially. Yet the ability of caregivers to access and apply both science and complete patient information is

improving, secure and accurate. And we've invested \$4 billion to build and install a system that we believe this generation of patients and caregivers needs.

A health care crisis of communication.

Over the last 50 years medical science has advanced exponentially. Yet the ability of caregivers to access and apply both science and complete patient information is repeatedly impeded by the paper system that contains it. Patient data typically sits in static, inert and functionally truncated paper records. Paper medical records are often incomplete and out of date. Sharing evidence, research findings and simple patient information is usually an arduous, inconsistent and often inaccurate task when paper records produce the data.

be self-evident. Full and secure access to data will give physicians visibility into patient status and health history, improving diagnosis and delivery of care. Information retrieval that took days, will take minutes. Or less.

The future system should open unprecedented new diagnostic tools. Physicians should be able to instantly share imaging and test results with colleagues across the hall or across the country. Patients should have instant access to their own records and be able to send, transmit or carry it from one provider to another. Secure, computerized data sharing can reduce errors, redundancies, lost information and costs.

A culture of continuous learning and connected care. Today, we're a mobile and connected society in everything except healthcare. At Kaiser Permanente we believe in a future healthcare system where patient information is accessible, instantaneous, constantly

20,000 secure e-messages between clinicians and patients every single day.

Maximizing information for the clinician means optimizing care for the patient. Done well, we believe a computerized care support system can help both to restore and enhance each physician's original mission. The right system provides more time with patients, better information about care and less time with traditional paperwork. The right system also needs to be focused on the patient's need for affordable, well informed, customized and compassionate care. We believe new computer systems are needed to lead our nation's health care reform agenda into the 21st century. For us, right now, it's a work in progress and progress is being made.

Get more information at kp.org/future



Meaningful Use Incentives:

- Safety, effectiveness
- Patient engagement
- Continuity of care
- Population health
- Private, secure

*Kaiser Permanente full page ad in "Washington Post," 2008



Four Primary Dimensions to Consider





Personal Health Information & Data Sharing

- ❑ Personal access to physiologic and clinical data contributes to a culture of health and better self-management.
- ❑ Personal health data are massively generated and collected from devices attached to and within the body under control of the individual.
- ❑ Patients are secure with informed consent in sharing data with designated health care professionals and researchers.



PRECISION MEDICINE INITIATIVE

Pioneer **a new model for doing science** that emphasizes **engaged participants, responsible data sharing, and privacy protection.**



Person- & Family-Centered Care

- ❑ Healthcare has transformed to a fully patient- and family-centric system with patient and family values as core components to any care plan for cancer.
- ❑ Patients report feeling:
 - more “connected” to their cancer care providers.
 - that help is just a mouse click or smartphone call away.
 - that most providers have equal access to vital life-saving information available in their records.





Devices, Sensors, & Apps

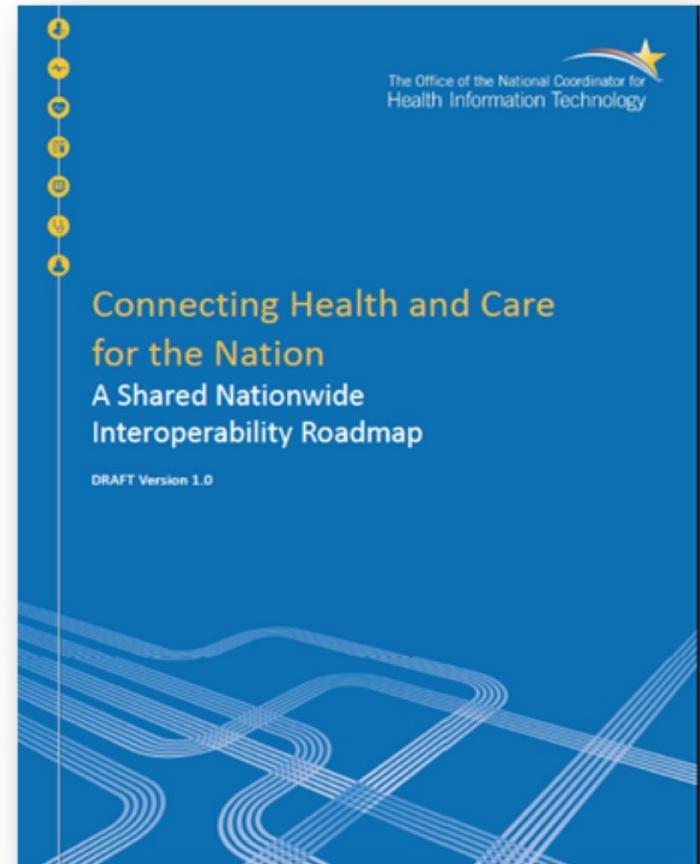
- ❑ Mobile computing reaches 85% of the US population by 2020 with broad adoption across race, ethnicity, region, or literacy level.
- ❑ Just-in-time, adaptive interventions become ubiquitous and accessible through a vibrant ecosystem of evidence-based, interoperable apps.





National Health Information Infrastructure

- ❑ ONC reaches its **2020** goal of an interoperable infrastructure for data flow controlled by individuals.
- ❑ Cancer prevention, control, treatment, and survivorship improve, with greater connectivity and fewer discontinuities.





2014-2015 Series Outcomes



Review and discuss content from workshops with series co-chairs.



Conduct additional research needed.



Write report to the White House.



2014-2015 Series Outcomes

The Panel will make **specific, actionable recommendations** relevant actors can take to facilitate interaction with an interoperable health system using connected health approaches.



Contact Us

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Towards a Federal Workforce in Hematology and Oncology



Reinventing the Federal Oncology Workforce:

Goal: Create Multilateral Benefit in a Joint Program to Recruit Combined FDA and NCI/CCR Clinical Investigators

- FDA gains an academic oncologist with disease-specific expertise who is actively involved and understands critical nuances of the field
- NCI gains a clinical investigator and leader who understands regulatory considerations in drug development
- The oncologic community gains a regulator/academic who will provide a leadership voice to help design trials with regulatory endpoints in mind.

A Joint Program Recruiting Clinical Investigators

for combined FDA/CCR Positions

- Combined recruiting effort by:
 - FDA Center for Drug Evaluation and Research (CDER)/ Office of Hematology and Oncology Products (OHOP)
 - NCI-Center for Cancer Research (CCR)
- 3 FDA/CCR Investigator positions
- Joint appointment at NCI and FDA; FDA employee
- Time divided between clinical and regulatory duties



Investigators will serve in two capacities:

Associate Office Director for Clinical Research (FDA)

Principal Investigator (NCI)

- At FDA: become an expert in regulatory processes focusing on a specific disease type, from IND to NDA and post-marketing; develop a pivotal role in guiding industry and academia in their approach to drug development.
- At NCI: collaborate with existing clinical teams for the development and execution of clinical trials, enrollment and treatment of patients, analysis and publication of data; serve as a sounding board for clinical trial design.

FDA/CCR Investigators: What We Seek

- Mid-Career Clinical Investigator with clinical trial experience
 - 5 – 10 years post fellowship
 - American Board of Internal Medicine Subspecialty Board Certified
- Expertise in a particular disease area in hematology/oncology
- Academic level: Associate Professor/Professor
- Prioritizes maintaining an active clinical research career
- Interested in developing regulatory expertise in oncology, with an opportunity to influence academic and industry approaches to drug development

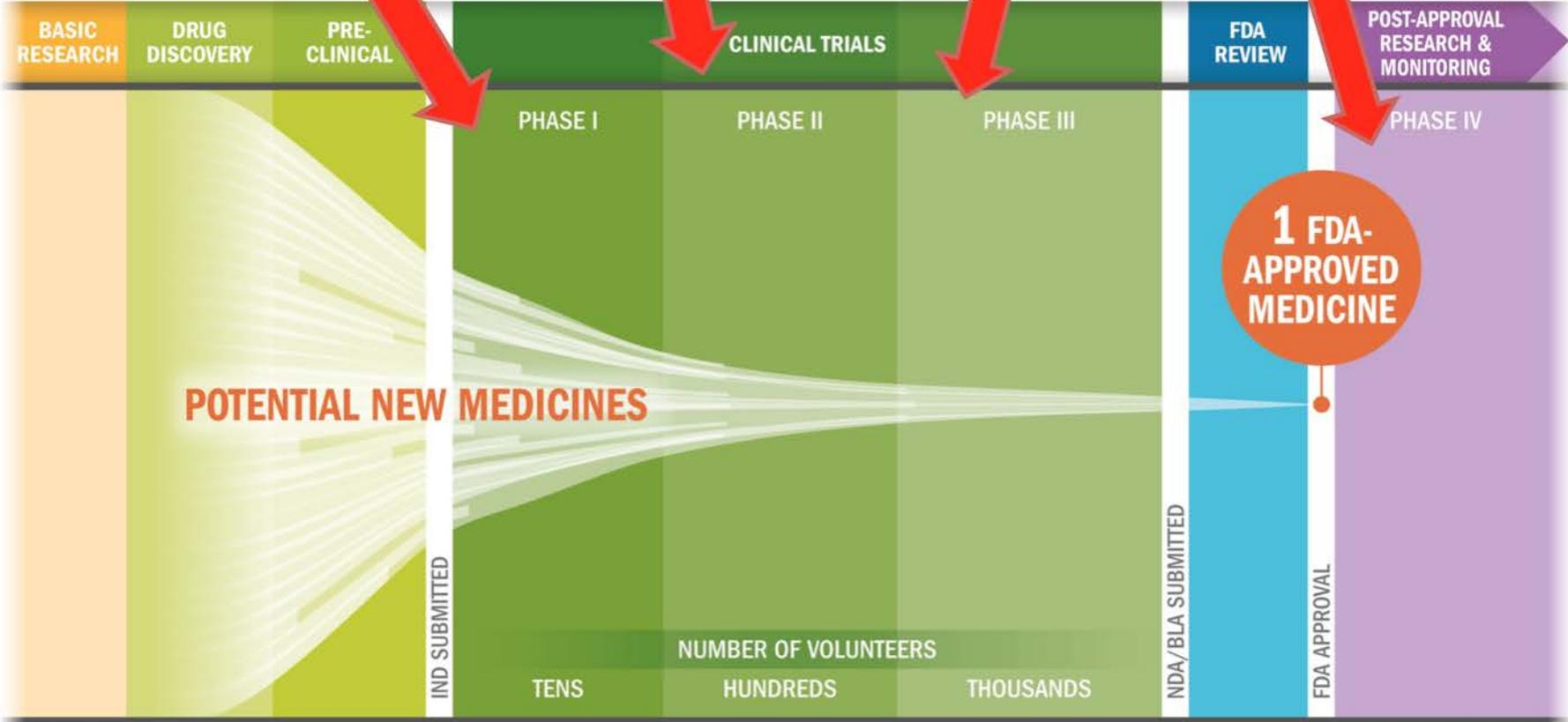
Clinical Regulatory Pathway: Then

Safe dose

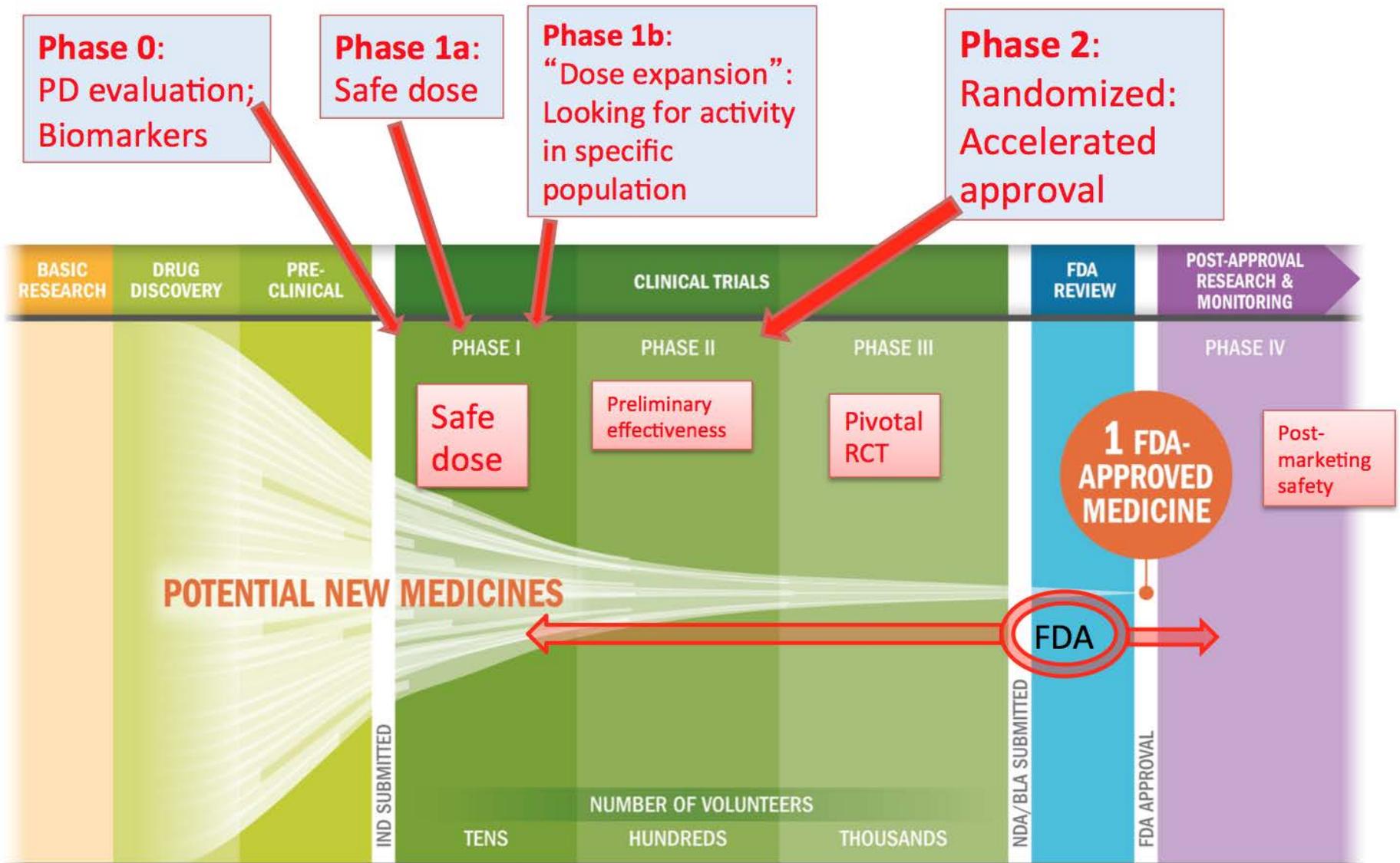
Preliminary effectiveness

Pivotal RCT

Post-marketing safety



Clinical Regulatory Pathway: Now

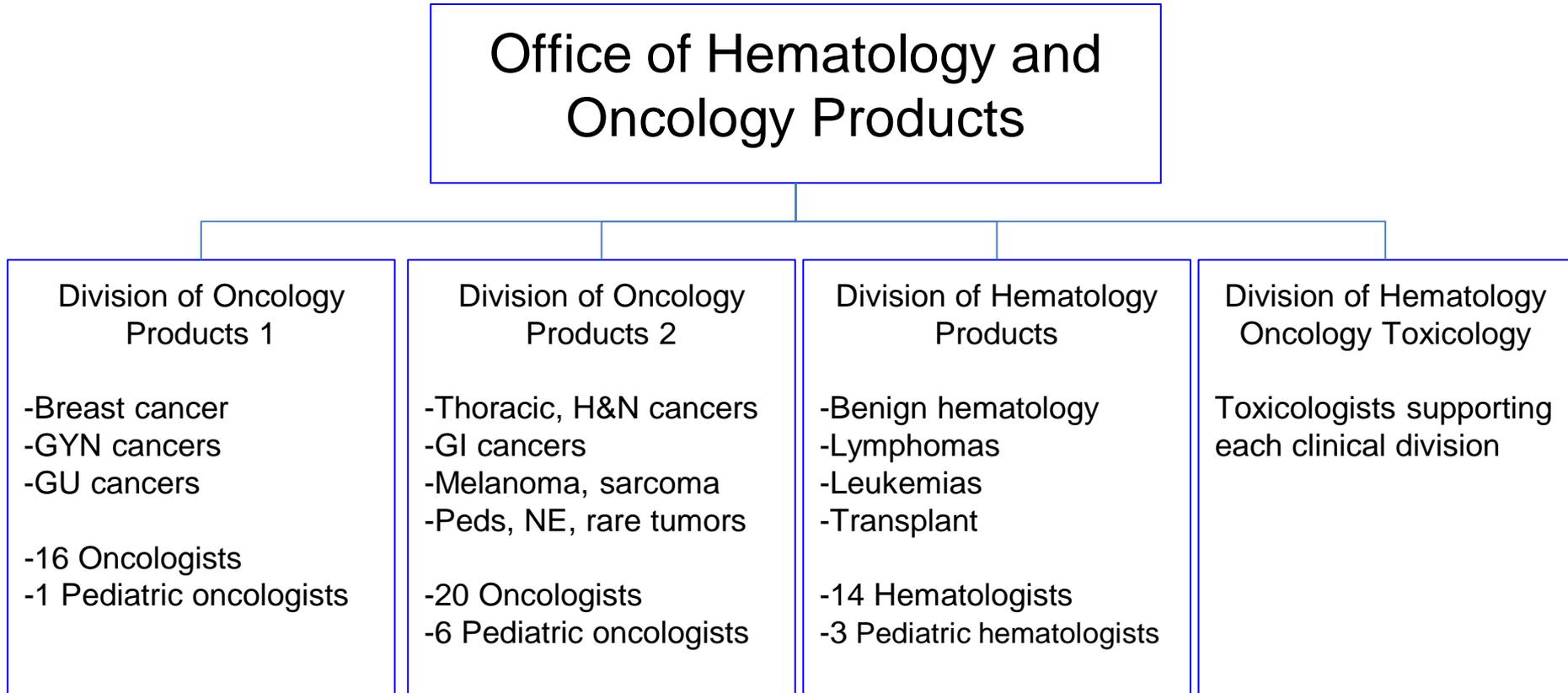


Office of Hematology and Oncology Products, FDA

- Located in Silver Spring Maryland
- Almost 200 employees including medical and pediatric hematologists/oncologists and other physicians, nurse practitioners, pharmacologists, toxicologists and support staff.
- Work very closely with other centers, divisions and offices with an array of scientists including biostatistics, chemists, physicists, and others throughout the FDA

Reorganized in 2011 into disease-specific divisions, modeled after academic setting
→ to provide more nuanced support for clinical trial design and drug development

Reorganization was instrumental in creating a new drug development environment





Associate Director,
Clinical Research, OHOP, FDA



- Regulatory training within the context of a multidisciplinary disease-specific regulatory team
- Develop expertise in the application of federal drug regulations in a specific therapeutic area
- Oversee a portfolio of drug and biologic products at all phases of development
- Lead meetings with industry and academic sponsors, providing regulatory and trial design advice



Associate Director, Clinical Research, OHOP, FDA



- Lead meetings with industry and academic sponsors, providing regulatory and trial design advice
- Represent FDA to external stakeholders, including academia, industry, and patient advocacy organizations at national and international meetings
- Opportunity to conduct and publish regulatory science, leveraging exclusive data and computing resources available at FDA
- Must recuse themselves from regulating products used in trials

Principal Investigator at the NCI's Center for Cancer Research (CCR)

- Investigators will collaborate with a team & clinic in the CCR
- Investigators will develop and submit clinical trials – within framework of clinical branch agenda and patient population
- Scientific review of clinical trials will follow CCR SOP
- An estimated 2 - 4 actively accruing clinical trials per PI
- Investigator will participate in teaching
- Clinical activities fully funded
- Conduct investigator-initiated, industry, & cooperative group studies



Clinical Oncology Branches in the CCR

1. Genitourinary Malignancy Branch
2. Thoracic and GI Oncology Branch
3. Developmental Therapeutics Branch
4. Women's Malignancies Branch
5. Lymphoid Malignancies Branch
6. Dermatology Branch
7. Experimental Transplantation and Immunology Branch
8. HIV and AIDS Malignancy Branch
9. Vaccine Branch
10. Radiation Oncology Branch
11. Pediatric Oncology Branch
12. Urologic Oncology Branch
13. Endocrine Oncology Branch
14. Surgery Branch
15. Neuro-Oncology Branch



Center for Cancer Research: Unmatched Protocol Support

- Center for Cancer Research has centralized much of the clinical trial infrastructure
- Protocol Support Office: Services at all stages of protocol lifecycle
 - Help with drafting LOIs and Protocols
 - Support for Scientific Review process
 - Drafting and submission of IND's
 - FDA submission
 - IRB submissions
- Tech Transfer: An office for agreements with industry partners; submission of patent applications
- Research Nursing: Highly skilled research nurses well versed in Good Clinical Practice
- Clinical Care: Medical Oncology fellows in clinic; nurse practitioners in clinic and in hospital
- Core Facilities: Intramural laboratories specializing in assays of biologic endpoints
- Basic Science: Intramural basic science laboratories eager to collaborate
- Data Management: Centralized data management provides highly skilled data managers to support data entry and downloads, and continuing review and other regulatory submissions

A Vision for the FDA/NCI Collaboration:

- FDA/CCR Clinical Investigator a leader in the whole academic community
- Some leadership roles these investigators could play at **FDA**:
- Bring disease-specific expertise to the FDA
 - Awareness of finer issues in each particular disease
 - Interaction with cooperative groups
 - Outreach with advocacy groups
- Push unmet clinical needs at the FDA, e.g.
 - CNS metastases
 - Fertility and other survivor issues
 - Integrate real-world data
 - Liaise with NCI and FDA on mission-critical programs, e.g. NCI-MATCH
- Advance efforts to modernize clinical trial design to align with the clinical community
 - Data collection standards

A Vision for the FDA/NCI Collaboration:

- FDA/CCR Clinical Investigator a leader in the whole academic community
- Some leadership roles these investigators could play at **NCI**:
- This person could help design trials that establish and use new regulatory endpoints:
 - Alternatives to the gold standard, overall survival
 - Alternatives to the current surrogates, PFS, ORR
 - e.g. Kinetic analyses
 - Alternatives to the current dose-finding schema,
 - e.g. Continuous Reassessment Model
 - Challenge or expand currently accepted inclusion criteria
 - Highlight regulatory considerations in individual trials
- Continue academic activities
 - Education of fellows
 - Serve on editorial boards
 - Serve as attending staff in the NIH Clinical Center

Logistics and Application

- FDA will serve as chair of search committee; CCR will participate in search and selection
- During recruitment, each candidate will identify a clinical branch with mutual interest; meet and discuss areas of mutual interest with CCR Branch Chief
- Questions? Contact: NCI: Dr. Susan Bates 301-496-5941, FDA: Dr. Sanjeeve Bala 240-402-4975

Please send inquiries and CV to:

Richard Pazdur, MD
Director, Office of Hematology and
Oncology Products
Richard.Pazdur@fda.hhs.gov

Susan Bates, MD
Head, Molecular Therapeutics
Group, NCI
Batess@helix.nih.gov

NCI Cancer Centers Working Group

Phase II: Streamlining the CCSG Application and Evaluation Process

**Joint NCAB/BSA
June 24, 2015**

Membership

- Mary Beckerle, PhD (Huntsman/Utah), Co-Chair
- Brian Springer, MHA (Moffitt), Co-Chair
- Frederick Appelbaum, MD (Fred Hutchinson) 9 Center Dir.
- Kevin Cullen, MD (Greenebaum/Maryland) 4 Assoc. Dir. Admin.
- Chi Dang, MD, PhD (Abramson/Pennsylvania)
- Robert Gerlach, MPA (Norris Cotton/Dartmouth) 3 NCI Staff
- Stanton Gerson, MD (Case Western)
- Lauren Hackett, MPA (Vanderbilt-Ingram)
- Anita Harrison, MPA (Hollings/Med Univ of South Carolina)
- Michelle LeBeau, PhD (Univ of Chicago)
- Craig Thompson, MD (Memorial Sloan-Kettering)
- Kristiina Vuori, MD, PhD (Sanford-Burnham)
- George Weiner, MD (Holden/Iowa)
- Sonya Roberson, PhD (NCI) - Liaison
- Shamala Srinivas, PhD (NCI) - Liaison
- Linda Weiss, PhD (NCI) – Executive Secretary

Goals

- Enhance CCSG application and review process
- Amplify referee ability to assess impact and innovation
- Reduce administrative burden and streamline the process

Timeline

- April-May 2014
 - Preparation/planning and committee recruitment
- June-August 2014
 - 4 working subgroups
 - 8 team calls
 - E-mail dialogue
- September-October 2014
 - Final report/recommendations assembled
- December 11, 2014
 - Discussion at Subcommittee A “Parent Committee”
- February 9, 2015
 - Review at Center Director’s meeting

Recommendations in 4 Major Areas:

- 1. Explore value and enhance efficiency of the site visit**
- 2. Increase clarity of requirements and review criteria**
- 3. Streamline data collection**
- 4. Streamline annual CCSG progress report**

The Working Group also assembled a collection of specific suggestions for improvement of CCSG application and review guidelines. (Appendix document)

All final recommendations
were discussed & endorsed by
participants of

- ✓ Working Group (unanimously)
- ✓ Subcommittee A
- ✓ Center Directors

Summary of WG Recommendations

1. Explore Value & Efficiency of the Site Visit

--Evaluate impact and merit of site visit

- Document and collect metrics on the value of site visit
 - *Other mechanisms (U, P, etc) have eliminated site visits*
 - *Significant time and cost savings for Centers and NCI*
 - *Scoring impact may balance out*

– Eliminate site visit tours and poster presentations for Shared Resources

– Replace with Q&A session for Shared Resources

– *Parent committee comments:*

- *Teambuilding value of site visit for Centers*
- *Site visit provides opportunity to answer questions*

Recommendations

2. Increase Clarity of Requirement/Review Criteria

- Modify instructions and review criteria to eliminate redundancy
- Restore individual review of Shared Resources
 - eliminate current “grouping” approach
- Better define eligibility requirements for “comprehensive” designation while avoiding “one size fits all” approach
- *Parent Committee comments:*
 - *Redundancy has some value for reviewers*
 - *Individual review of Shared Resources is preferred*
 - *Added specificity may constrain Centers and reviewers*

Recommendations

3. Streamline Data Collection

- Make greater use of direct data acquisition methods for Data Tables to reduce administrative burden
 - Tap existing systems (e.g., CTRP, RePORTER)
- Use *electronically available resources for Biosketches*
 - *Consider My NIH Biosketch for non-key personnel*
 - *Enhance utilization of existing central NIH resources*
- *Parent Committee comments*
 - *No concerns raised*
 - *Several of these actions already underway*

Recommendations

4. Streamline Annual CCSG Progress Reports

- Simplify process for annual Progress Report
 - Reduce narrative length to emphasize key accomplishments & major changes
 - Provide annually updated Data Tables to enable Program staff to track progress
 - Annual Progress Reports are time-consuming to produce and don't have actionable consequences
 - NCI Office of Cancer Centers utilizes progress reports in many ways

- *Not discussed by the Parent Committee.*

Next Steps

- National Cancer Advisory Board review
 - today
- Final report to Dr. Paulette Gray, Division of Extramural Activities
- Office of Cancer Centers implementation

Implementation timeline

“When issued” update by OCC for elements not defined in the CCSG FOA

Progress report & site visit structure

CCSG FOA “Guidelines” reissue

September 2016

First new format CCSG submission

January 25, 2017

Discussion and vote

Precision Medicine Initiative for Oncology

*James H. Doroshow, M.D.
Deputy Director for Clinical and Translational Research
National Cancer Institute, NIH*

Precision Medicine Initiative

Proposed FY16 Support

Agency	\$ Million
NIH	200
• <i>Cancer</i>	70
• <i>Cohort</i>	130
FDA	10
Office of the National Coordinator for Health Information Technology	5
TOTAL	\$215

Precision Medicine Initiative: Oncology

What Problems Are We Trying to Solve?

- For most of its 70-year history, systemic cancer treatment has relied on drugs marginally more toxic to malignant cells than to normal tissues
- Molecular markers to predict benefit or understand therapeutic resistance in the clinic have usually been lacking

Proposed Solution to These Problems

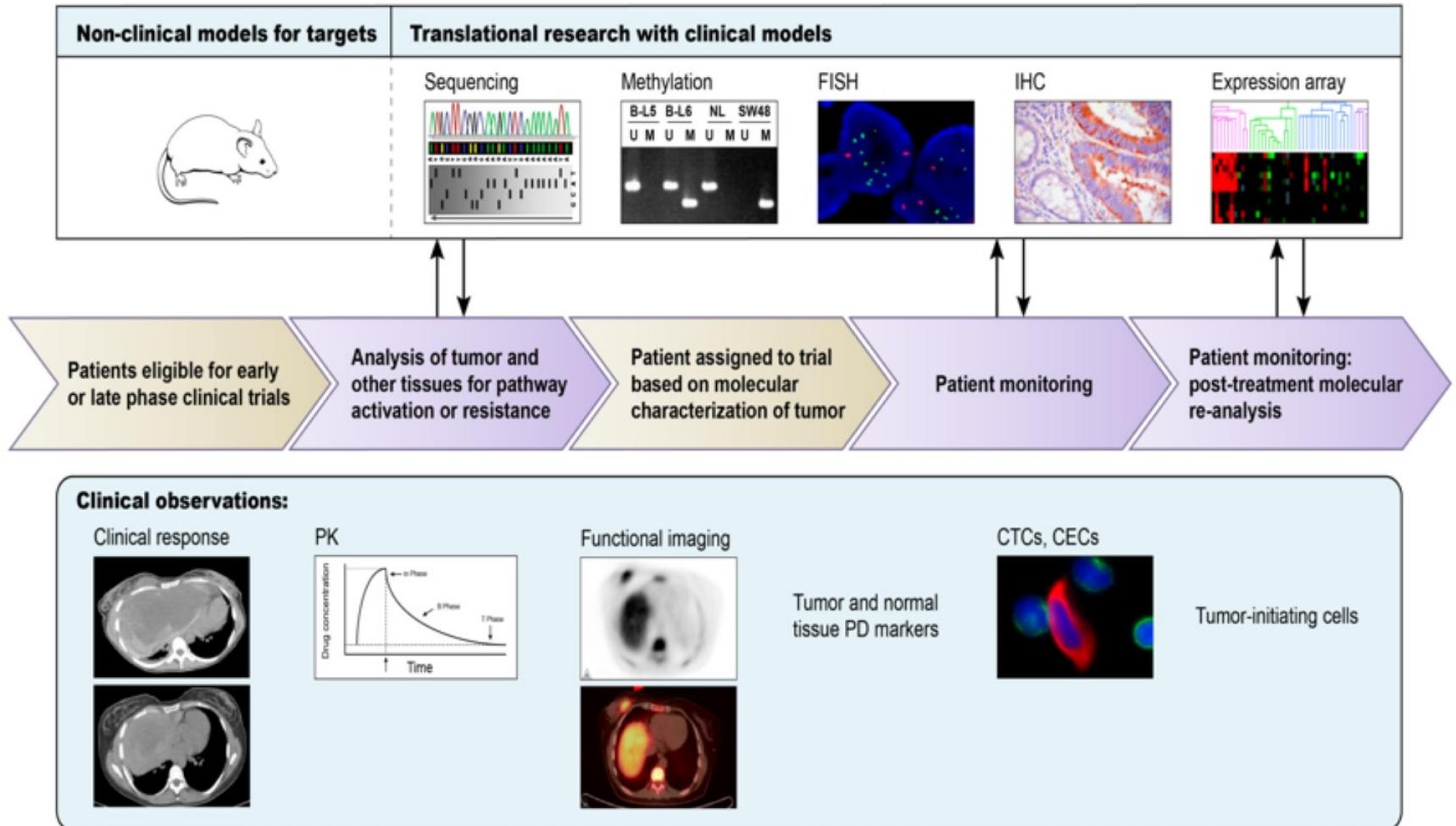
- Use genomics to identify and target molecular vulnerabilities of individual cancers

A Modified Definition of Precision Medicine

Interventions to prevent, diagnose, or treat a disease (e.g., cancer), based on a molecular and/or mechanistic understanding of the causes, pathogenesis, and/or pathology of the disease. Where the individual characteristics of the patient are sufficiently distinct, interventions can be concentrated on those who will benefit, sparing expense and side effects for those who will not.

Modified by D. Lowy, M.D. from: IOM's Toward Precision Medicine, 2011

Precision Medicine/Oncology in Practice



Precision Medicine Initiative: Oncology

Increase Genomics-Based Clinical and Preclinical Studies of Cancer Treatment

- Expand genomics-based clinical trials
- Understand & overcome resistance to targeted drugs; drug combinations; and mechanistic understanding of immunotherapy
- Repository of patient-derived pre-clinical models for evaluating targeted therapeutics: Lou Staudt
- National cancer database to integrate genomic information with clinical response and outcome: Warren Kibbe

Precision Oncology Trials Launched

2014:

MPACT

Lung MAP

ALCHEMIST

Exceptional Responders

2015:

NCI-MATCH

ALK Inhibitor

MET Inhibitor

NCI-MATCH: Features (1)

[Molecular Analysis for Therapy Choice]

- Foundational treatment/discovery trial; assigns therapy based on molecular abnormalities, not site of tumor origin for patients without available standard therapy
- Regulatory umbrella for phase II drugs/studies from > 20 companies; single agents or combinations
- Available nationwide (2400 sites)

Precision Oncology Trials Launched

2014:

MPACT

Lung MAP

ALCHEMIST

Exceptional Responders

2015:

NCI-MATCH

ALK Inhibitor

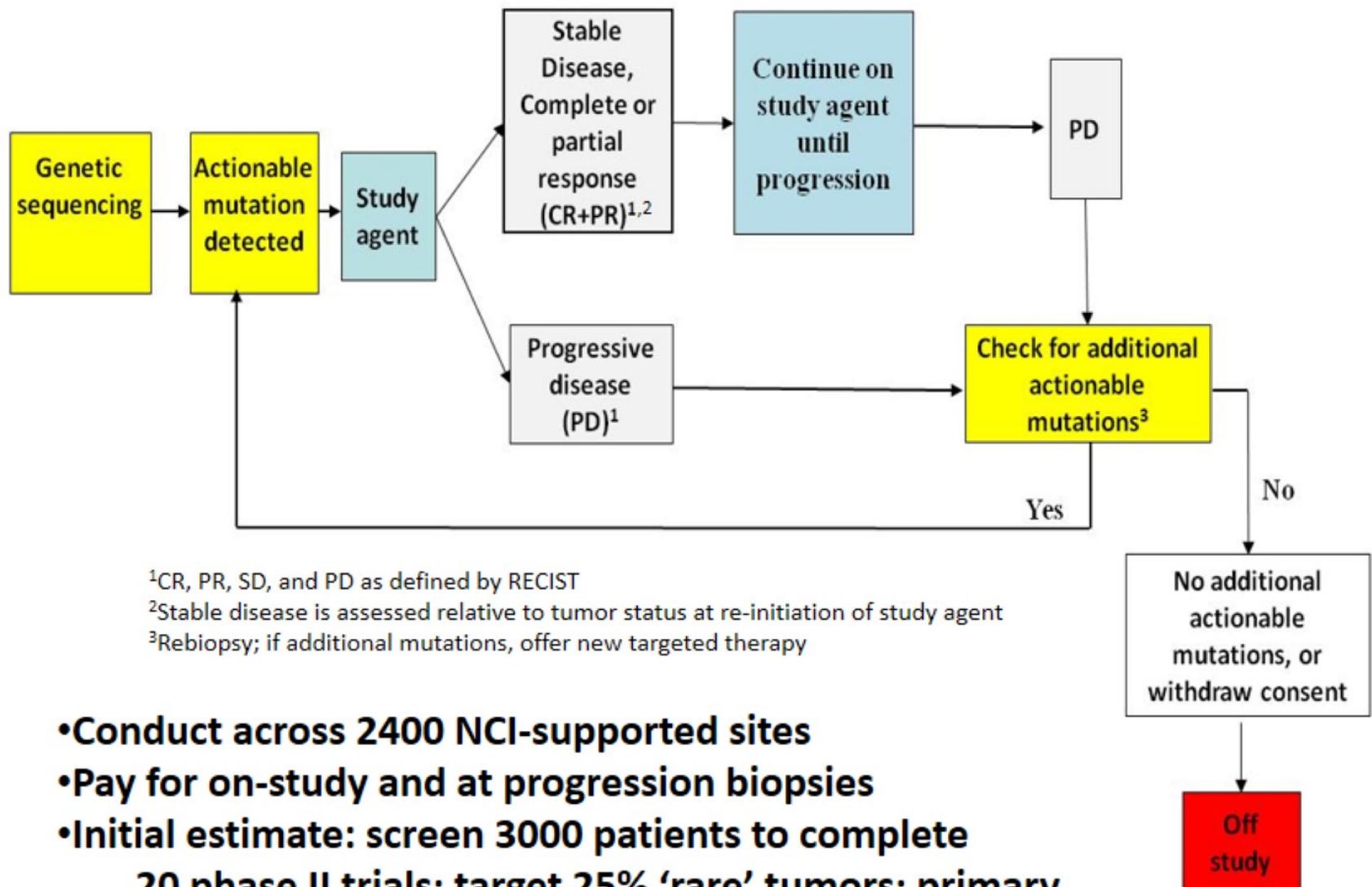
MET Inhibitor

NCI-MATCH: Features (2)

[Molecular Analysis for Therapy Choice]

- Validated and standardized gene sequencing at 4 sites; >96% concordance for “locked down” analysis of mutations in 143 genes using Ion Torrent PGM™ custom panel; fresh biopsies at study entry
- Co-developed by NCI and ECOG-ACRIN, part of NCTN; PI’s drawn from all network groups; trial planning by >150 clinical and pre-clinical scientists
- First patients to be entered July 2015

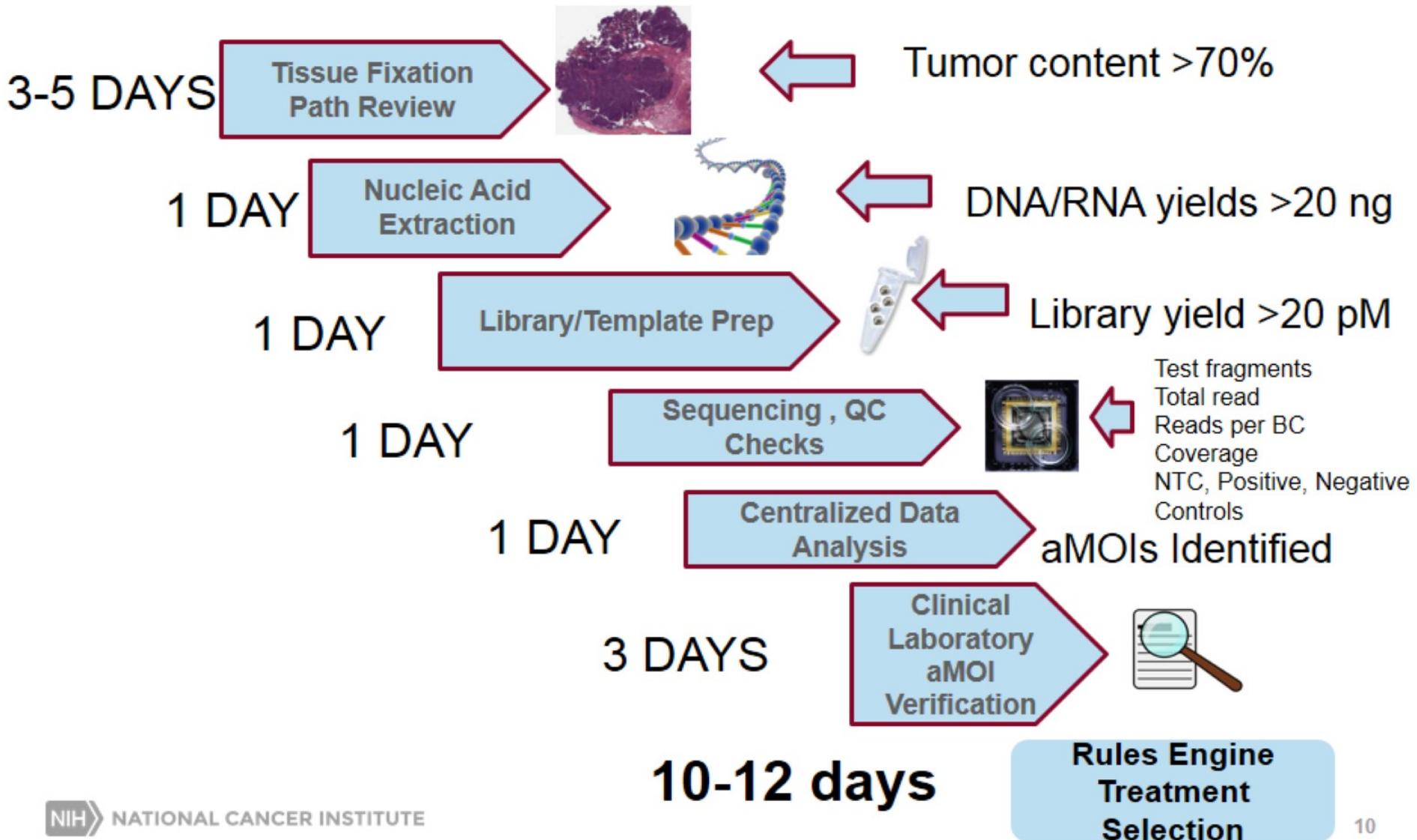
NCI MATCH



- **Conduct across 2400 NCI-supported sites**
- **Pay for on-study and at progression biopsies**
- **Initial estimate: screen 3000 patients to complete 20 phase II trials; target 25% 'rare' tumors; primary endpoint RR 5% vs. 25%**

MATCH Assay: Workflow for 10-12 Day Turnaround

Biopsy Received at Quality Control Center



NCI-MATCH: Initial Ten Studies

Agent(s)	Molecular Target(s)	Estimated Prevalence
Crizotinib	ALK Rearrangement (non-lung adenocarcinoma)	4%
Crizotinib	ROS1 Translocations (non-lung adenocarcinoma)	5%
Dabrafenib and Trametinib	BRAF V600E or V600K Mutations (non-melanoma)	7%
Trametinib	BRAF Fusions, or Non-V600E, Non-V600K BRAF Mutations (non-melanoma)	2.8%
Afatinib	EGFR Activating Mutations (non-lung adenoca)	1 – 4%
Afatinib	HER2 Activating Mutations (non-lung adenoca)	2 – 5%
AZD9291	EGFR T790M Mutations and Rare EGFR Activating Mutations (non-lung adenocarcinoma)	1 – 2%
TDM1	HER2 Amplification (non breast cancer)	5%
VS6063	NF2 Loss	2%
Sunitnib	cKIT Mutations (non GIST)	4%

Agents and targets below grey line are pending final regulatory review; economies of scale—larger number of agents/genes, fewer overall patients to screen

≈ 35%

PMI Oncology: Improving Cancer Treatment through Genomics

2006 -2014

TCGA

Targeted
Trials: MPACT,
ALCHEMIST,
Exceptional
Responders,
LungMAP

Oncogenic drivers of the
same tumor type
may be heterogeneous,
but same driver may be
found in several different
tumor types

2015

NCI-MATCH

*Announced June 1, Opens in July
throughout the US
(2400 sites)*

- Unprecedented & incorporates all tenets of precision medicine
- Treatment is based on genes and their mutations rather than on organ site

2015 & Beyond

THE PRECISION MEDICINE INITIATIVE FOR ONCOLOGY

ACCELERATING PROGRESS FOR PATIENTS

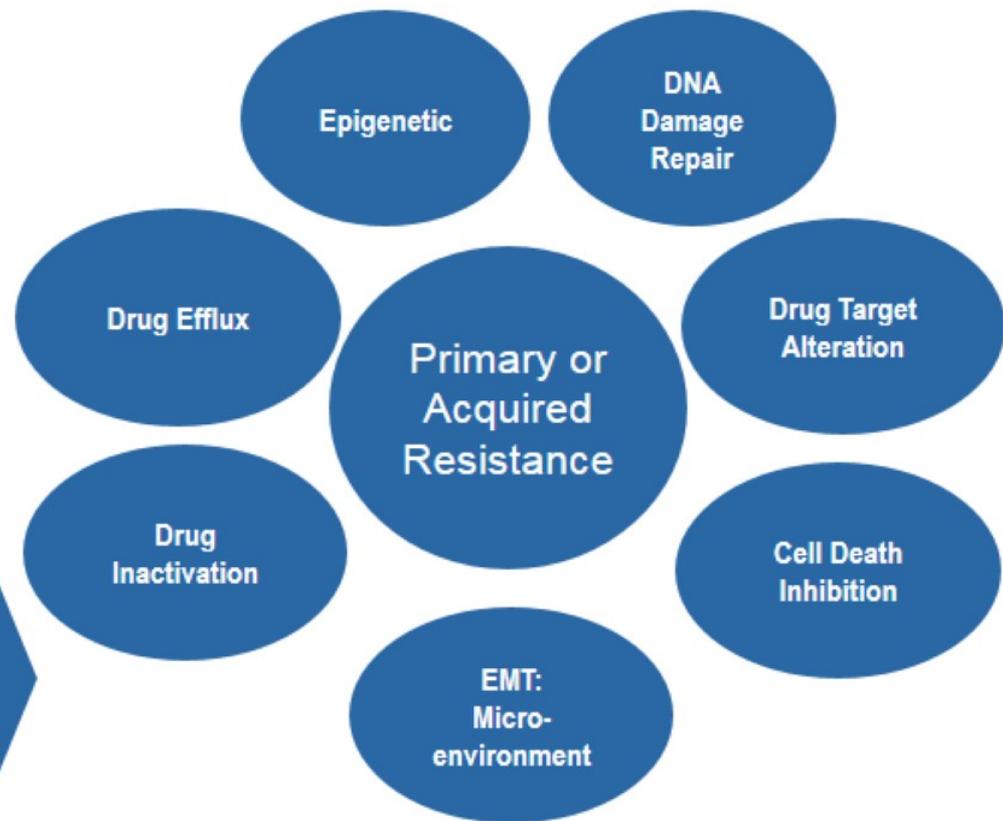
- Dramatically expand NCI-MATCH umbrella: to include new trials, new agents, new genes, and new drug combinations
- Increase mechanistic understanding of immunotherapy: to broaden its appropriate use
- Create a repository of patient-derived pre-clinical models and evaluate liquid biopsies: to improve understanding of cancer and drug resistance and to identify drug combinations that overcome resistance
- Establish a national cancer database integrating genomic information with clinical response and outcome: to accelerate understanding of cancer and improve its treatment

PMI for Oncology

Opportunities Enabled by PMI for Oncology: Expanding Genomically-Based Cancer Trials

- Accelerate Launch of NCI-Pediatric MATCH
- Broaden the NCI-MATCH Umbrella:
 - ✓ Expand/add new Phase II trials to explore novel clinical signals—mutation/disease context
 - ✓ Add new agents for new trials, and add new genes to panel based on evolving evidence
 - ✓ Add combination targeted agent studies
 - ✓ Perform Whole Exome Sequencing, RNAseq, and proteomic studies on quality-controlled biopsy specimens—extent of research based on resource availability
 - ✓ Add broader range of hematologic malignancies
- Perform randomized Phase II studies or hand-off to NCTN where appropriate signals observed
- Apply genomics resources to define new predictive markers in novel immunotherapy trials
- Expand approach to ‘exceptional responders’: focus on mechanisms of response/resistance in pilot studies

Mechanisms of Resistance To Targeted Cancer Therapeutics



- Broad range of mechanisms
- Until recently, tools to interrogate possibilities in vivo quite limited
- Resistance to single agents inevitable: 1^o or acquired; requires combinations but data to provide molecular rationale for the combination (both therapy & toxicity) not often available

Principles of Combination Therapy to Overcome Resistance: Then (1975) and Now (2015)

Cytotoxic

- Drugs are each active against the tumor in question (ORR)
- Drugs have different mechanisms of action to minimize resistance
- Drugs have different clinical toxicities to allow full dose therapy
- Intermittent intensive > continuous treatment for cytoreduction & to reduce immunosuppression

Cancer 35: 98, 1975

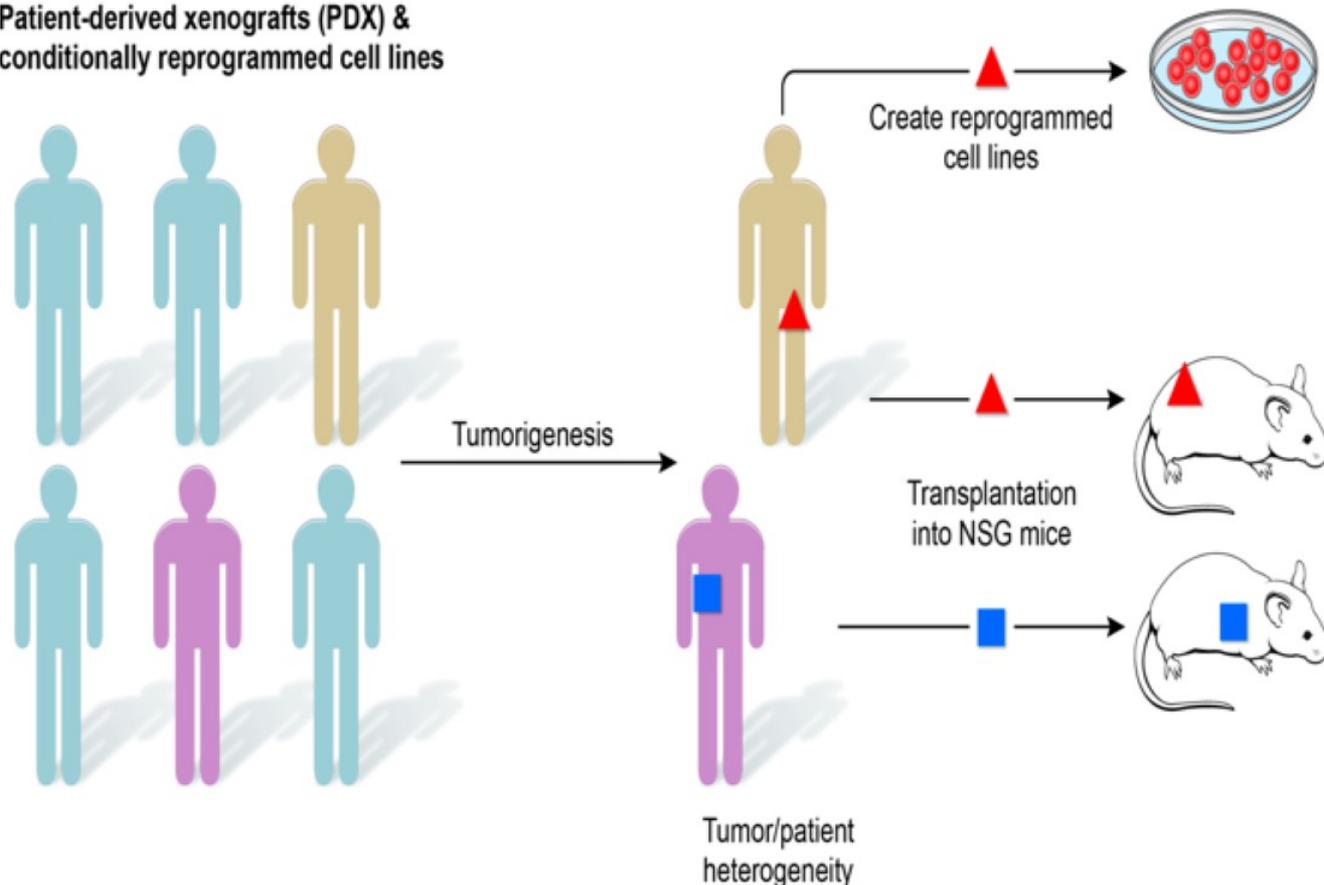
Targeted

- Agent has therapeutic effect on molecular pathway in vivo
- Agents have complementary effects on the same target or other targets in the same pathway or pathways that cross-talk to control tumor growth
- Toxicities not overlapping with cytotoxics & moderate to allow prolonged administration; consider physiological consequences of target engagement—strong relationship to toxicity profile
- Schedule to maximize target inhibition: Either continuous Rx or high dose to suppress target a reasonable goal

Needs Full Experimental Verification

New Patient-Derived Models for Precision Oncology to Study and Overcome Drug Resistance

Patient-derived xenografts (PDX) & conditionally reprogrammed cell lines

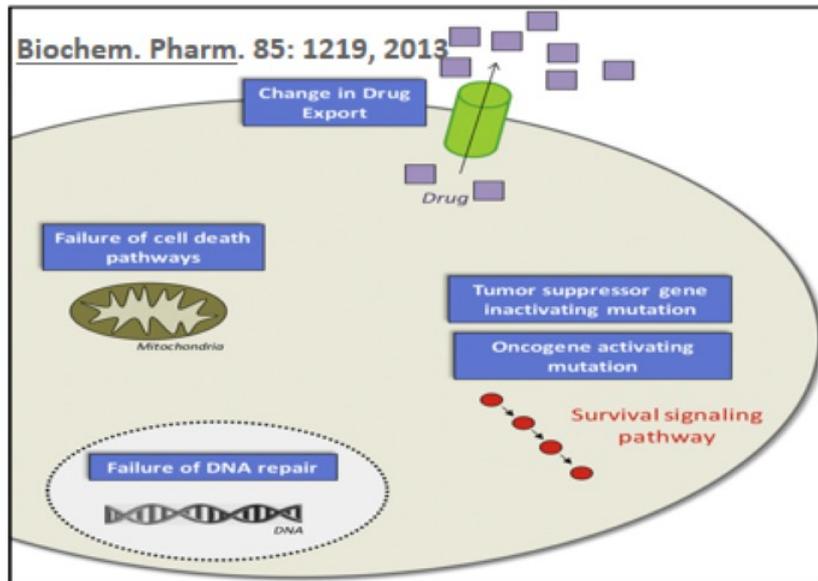


Molecularly characterize, treat/screen mice bearing transplants & cells with relevant drugs.

“Pre-clinical clinical trials”

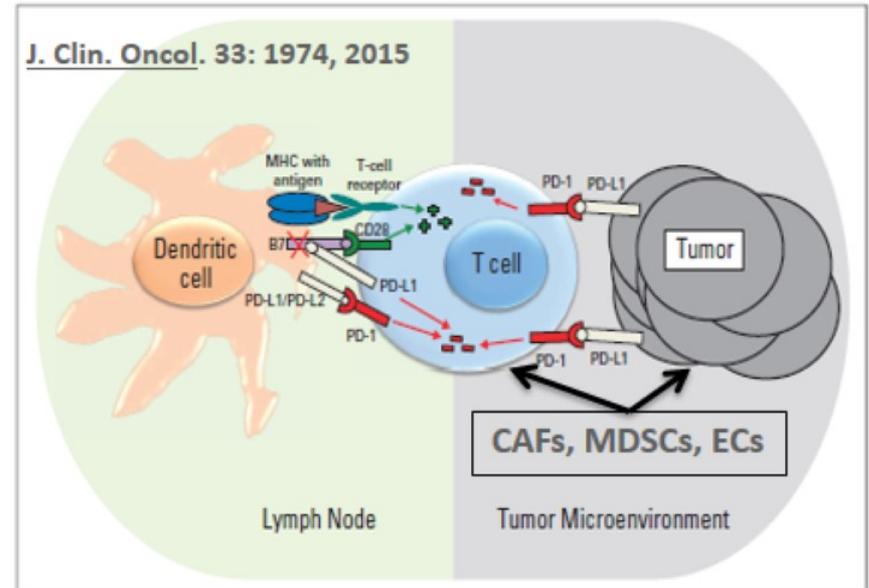
Precision Medicine Approaches to Overcoming Resistance: Opportunities

TUMOR CELL AUTONOMOUS



- Develop panel (>1000) of clinically annotated low passage organoids and conditionally reprogrammed lines for mutational evaluation, large scale systematic combinatorial drug screens, and resistance mechanism analysis
- On-study/at progression biopsies of NCI early phase trial patient cohort with resistant disease for molecular characterization (>500 pts/year); blood for CTC's, cfDNA, cfRNA, exosomes (liquid biopsies)

TUMOR MICROENVIRONMENT



- Develop complementary Patient-Derived Models: clinically-annotated PDXs from drug-resistant tumors
- Use for pre-clinical modeling of molecularly targeted combinations and for co-clinical trials of NCI-IND agents
- Genomic underpinnings of immunotherapeutic checkpoint control

Precision Medicine Initiative: Opportunities for Therapeutic Oncology

Developing Input from Extramural Community

- Organoids & Reprogrammed Cell Lines: Lou Staudt, M.D., **July 2015**
- Exceptional Responders Workshop—Next Steps: Barbara Conley, M.D., **Fall 2015**
- Immunotherapy—Combination Approaches and NGS: Helen Chen, M.D., **Fall 2015**
- PDX Models, Combination Therapy, and Drug Resistance: J. Doroshow, M.D. and Dinah Singer, Ph.D., **Fall 2015**
- Genomic Data Commons workshop: W. Kibbe, Ph.D., **Fall, 2015**



**NATIONAL
CANCER
INSTITUTE**

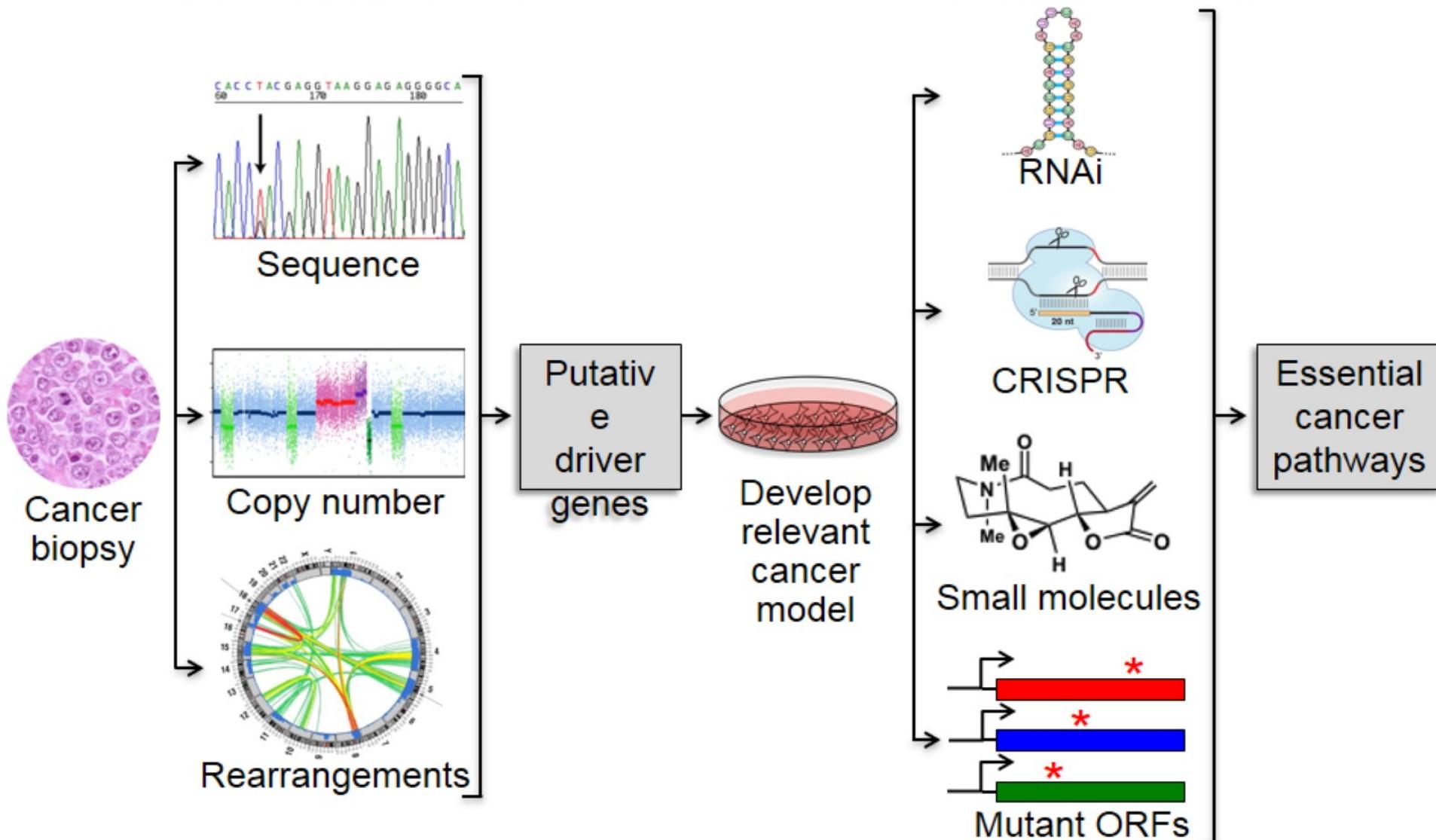
www.cancer.gov

www.cancer.gov/espanol

Development of Representative Human Cancer Model Systems Is Key to Identifying Essential Cancer Pathways

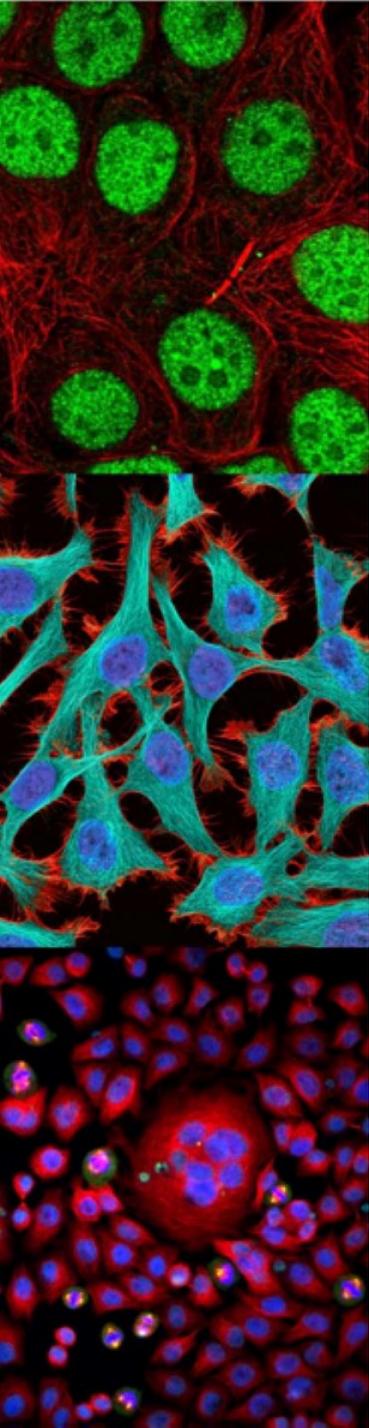
Structural genomics

Functional genomics



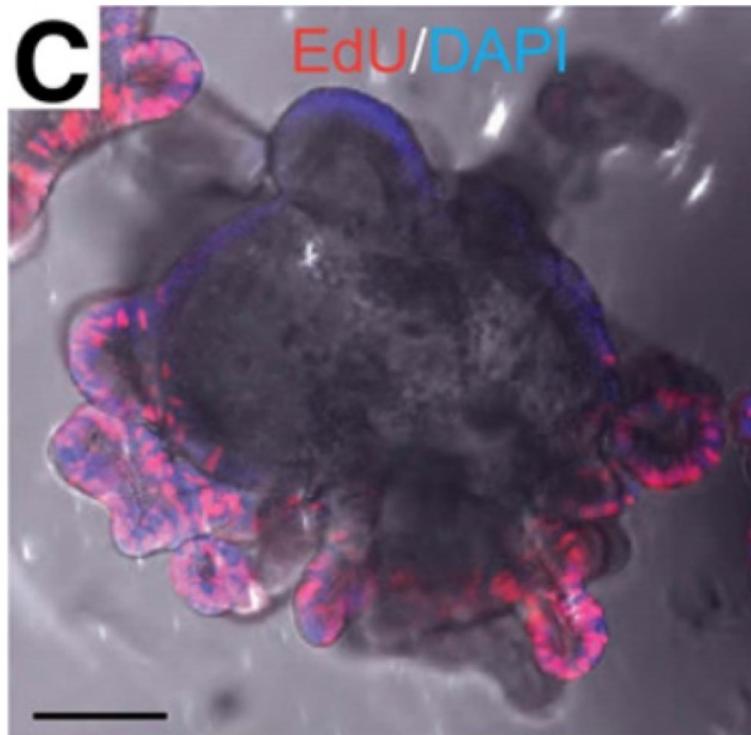
Modeling the Diversity of Human Cancer: An Unmet Need

- Genetic analysis has identified recurrent genetic lesions in cancer that range in frequency from 1% - >50% of cases.
- Most cancer cell lines have not been directly compared to the primary tumor using current genomic methods.
- Existing cell line models of common cancer types are suspect biologically and genetically (e.g. prostate CA)
- Models of rare cancer subtypes may be nonexistent or underrepresented
- Models do not exist for many recurrent genetic lesions in human cancer, and for common combinations of lesions
- Existing models do not recapitulate hierarchical relationships of tumor subpopulations (i.e. tumor propagating cells, stroma)



New Cell Culture Technologies Enable the Propagation of Normal and Malignant Epithelial Cells

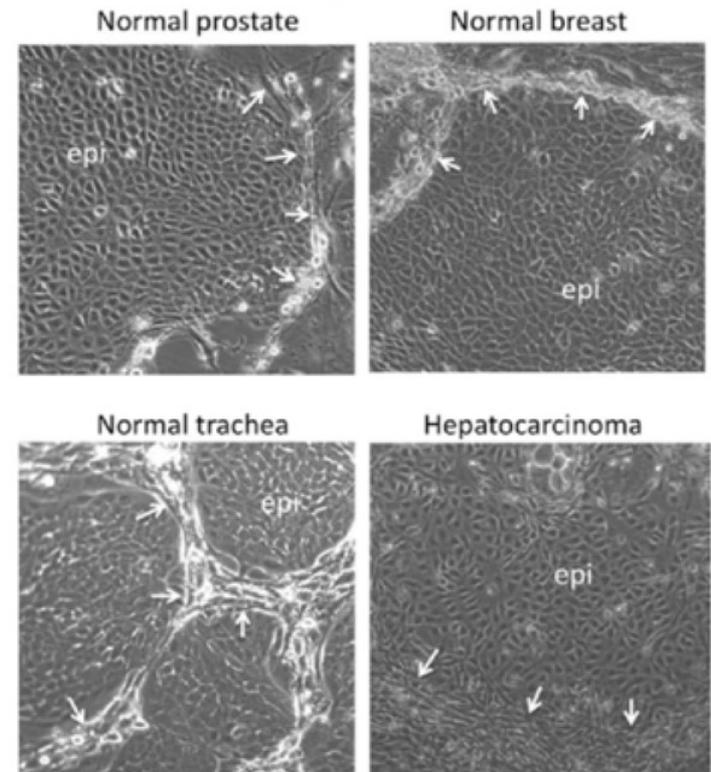
Organoid cultures



Clevers laboratory

Sato et al. *Gastroenterology* 2011 141:1762

Conditionally reprogrammed cells (CRCs)



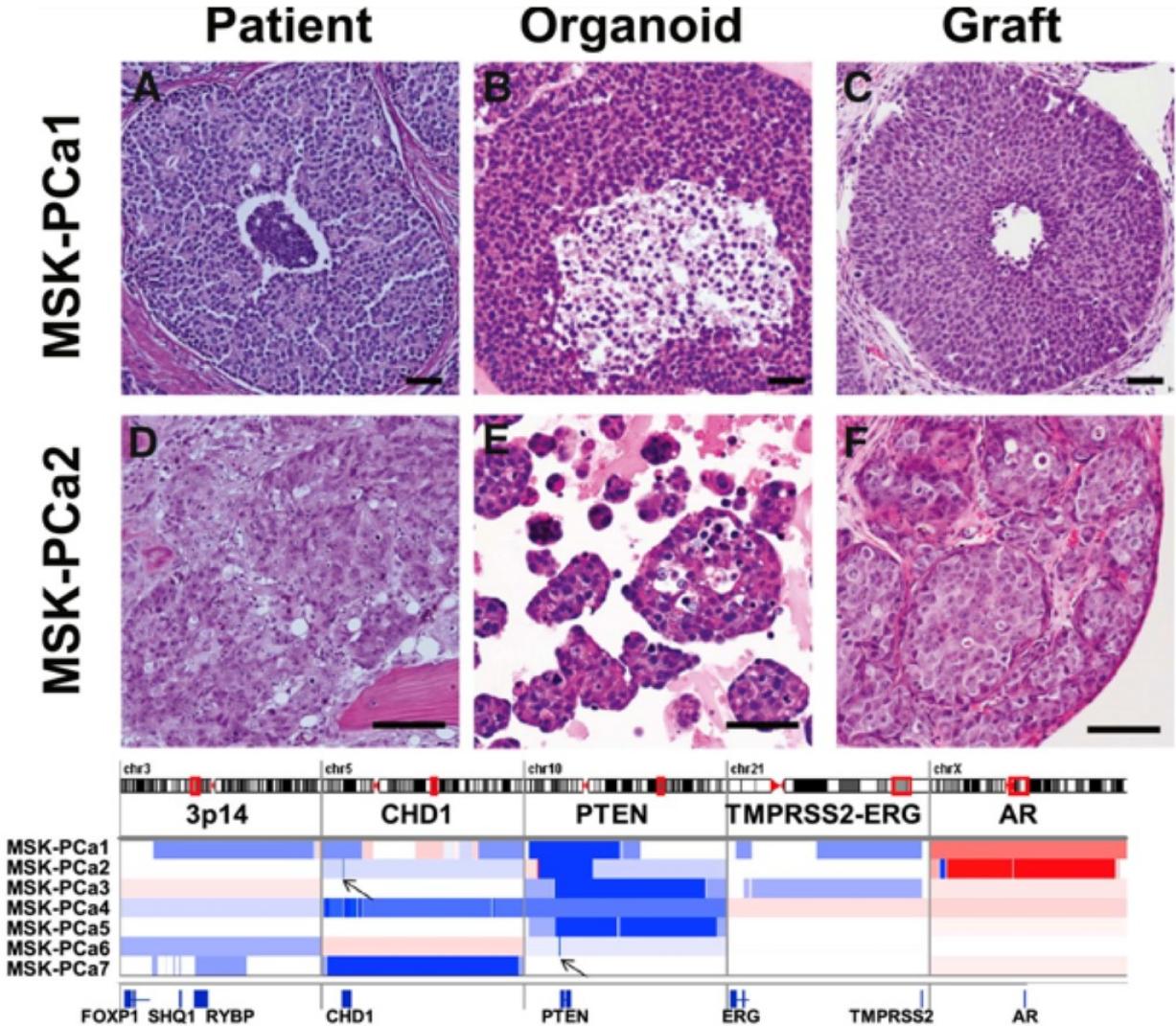
Schlegel laboratory

Liu et al. *American J Pathol* 2012 180:599

Human Cancer Model Initiative Endpoints

- Cancer genetics
 - Models that represent known driver lesions
 - Models that recapitulate pathway dependencies
 - Models that can be manipulated to address genetic contribution to the malignant phenotype

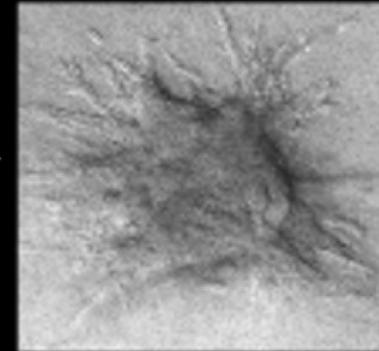
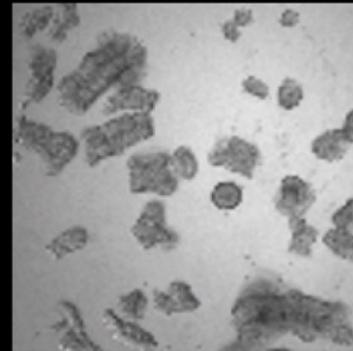
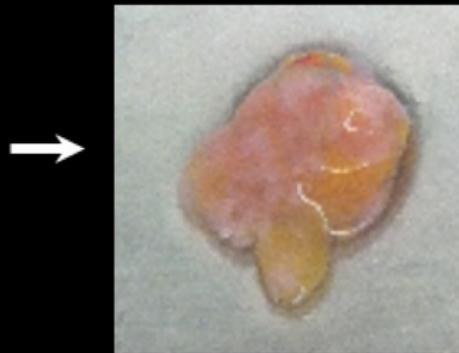
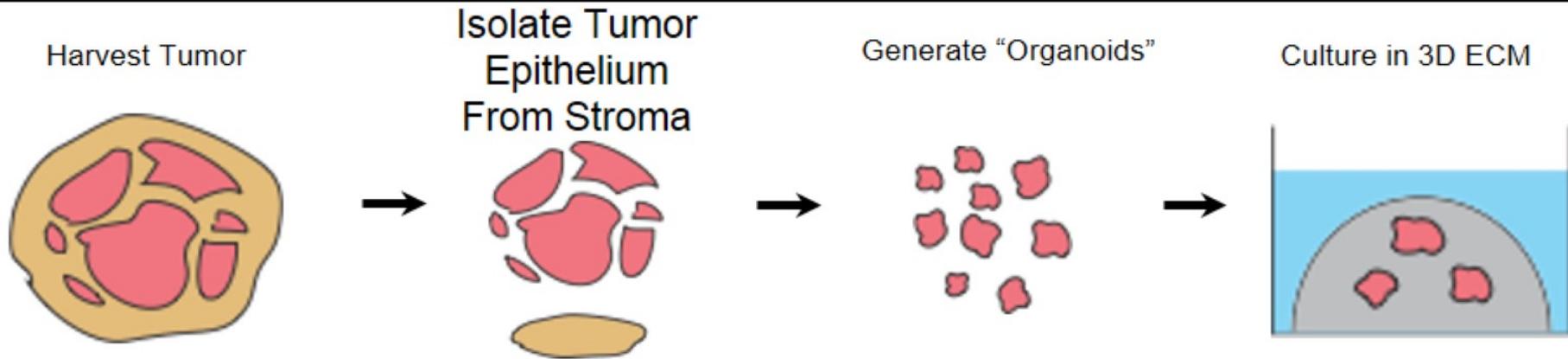
Organoids Capture Recurrent Genetic Lesions in Human Prostate Cancer



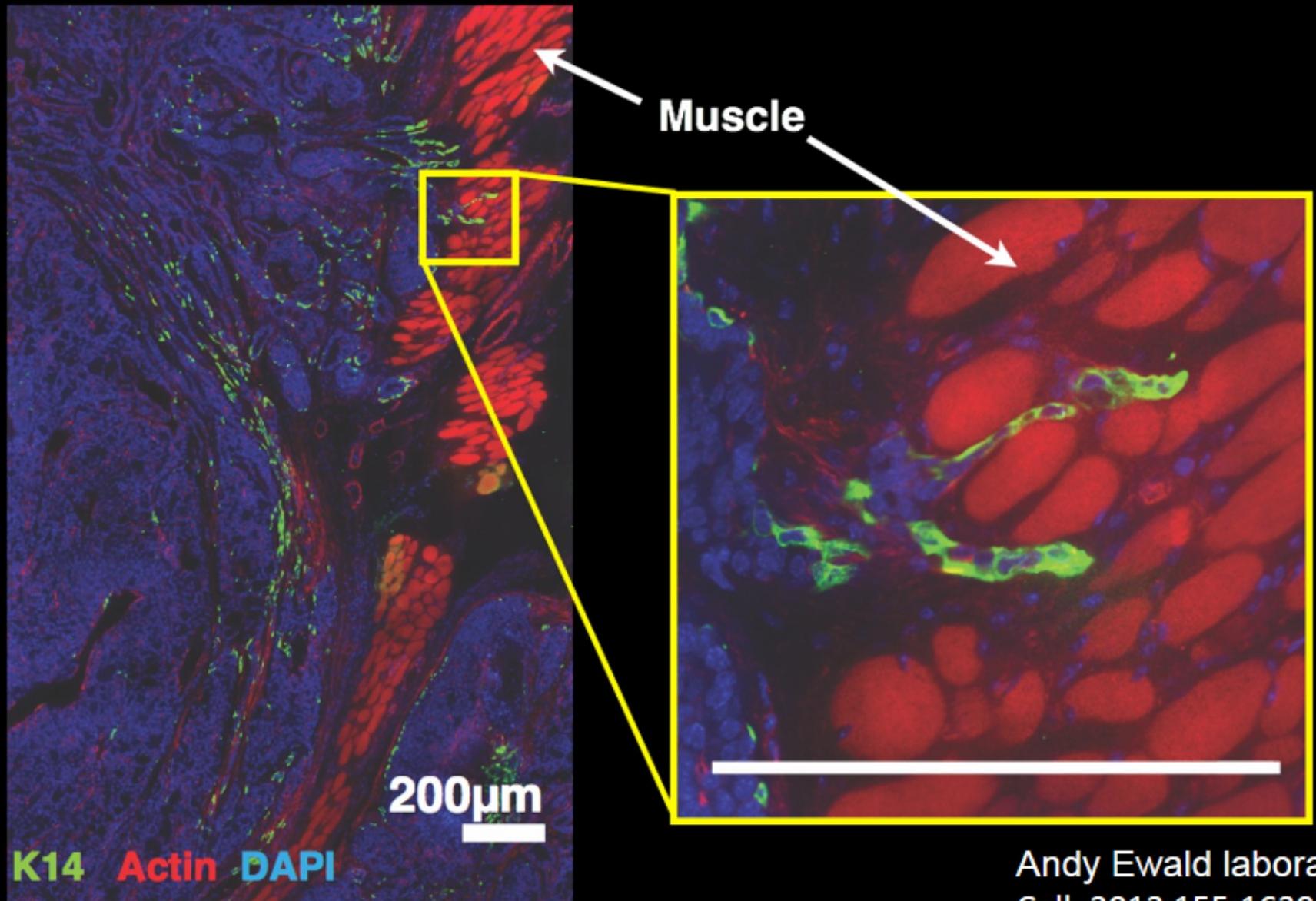
Human Cancer Model Initiative Endpoints

- **Cancer genetics**
 - Models that represent known driver lesions
 - Models that recapitulate pathway dependencies
 - Models that can be manipulated to address genetic contribution to the malignant phenotype
- **Cancer biology**
 - Models that recapitulate human cancer phenotypes
 - Dependencies on stroma
 - Metastatic propensity

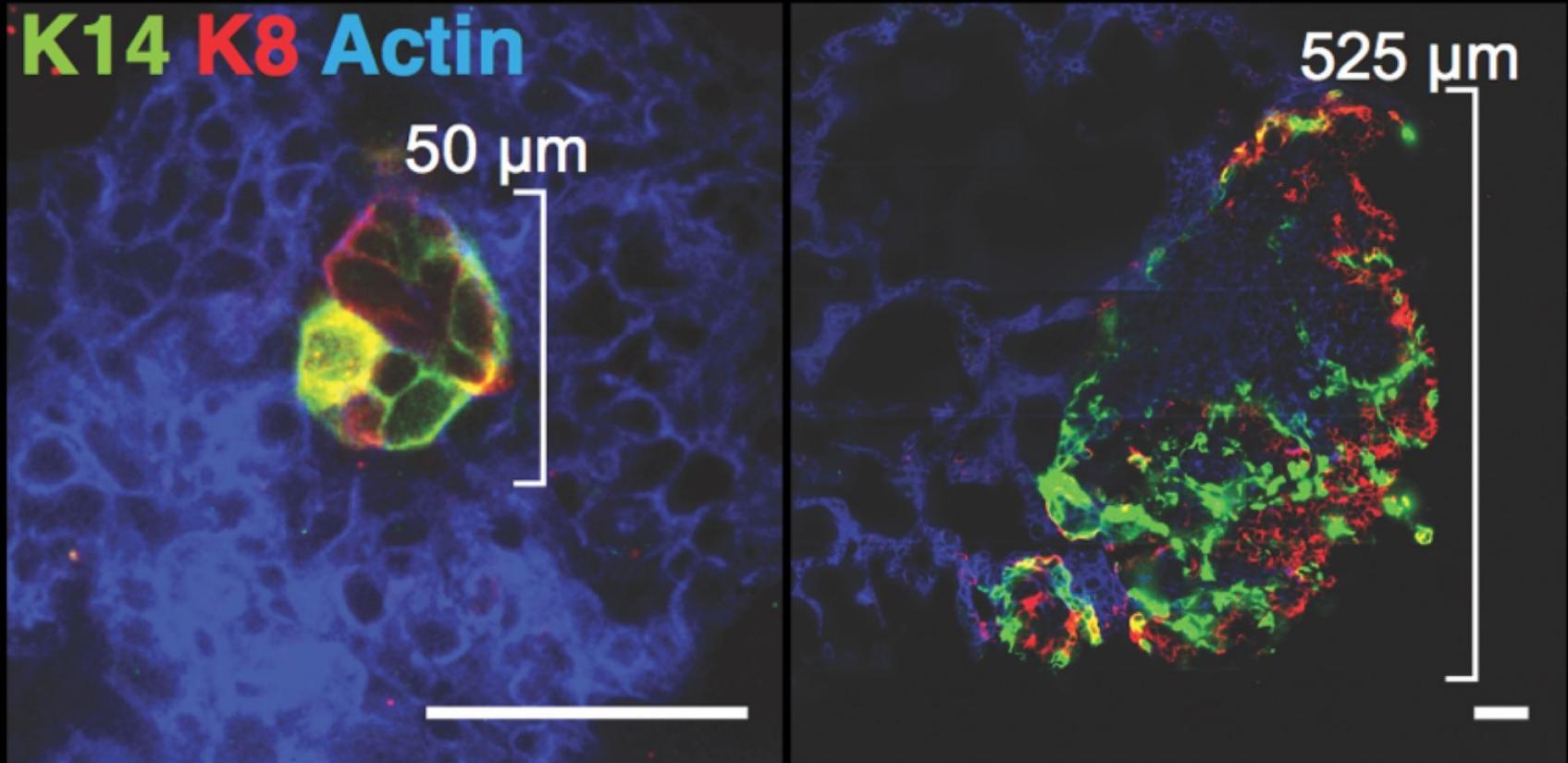
Generation of Tumor Organoids From Primary Human Breast Tumors



K14+ Cells Constitute 1.5% Of Tumor Cells And Lead 90% Of Invasion Events In Vivo



K14+ Cells Constitute 1.5% Of Primary Tumor Cells And Are Present In 90% Of Metastases In Vivo

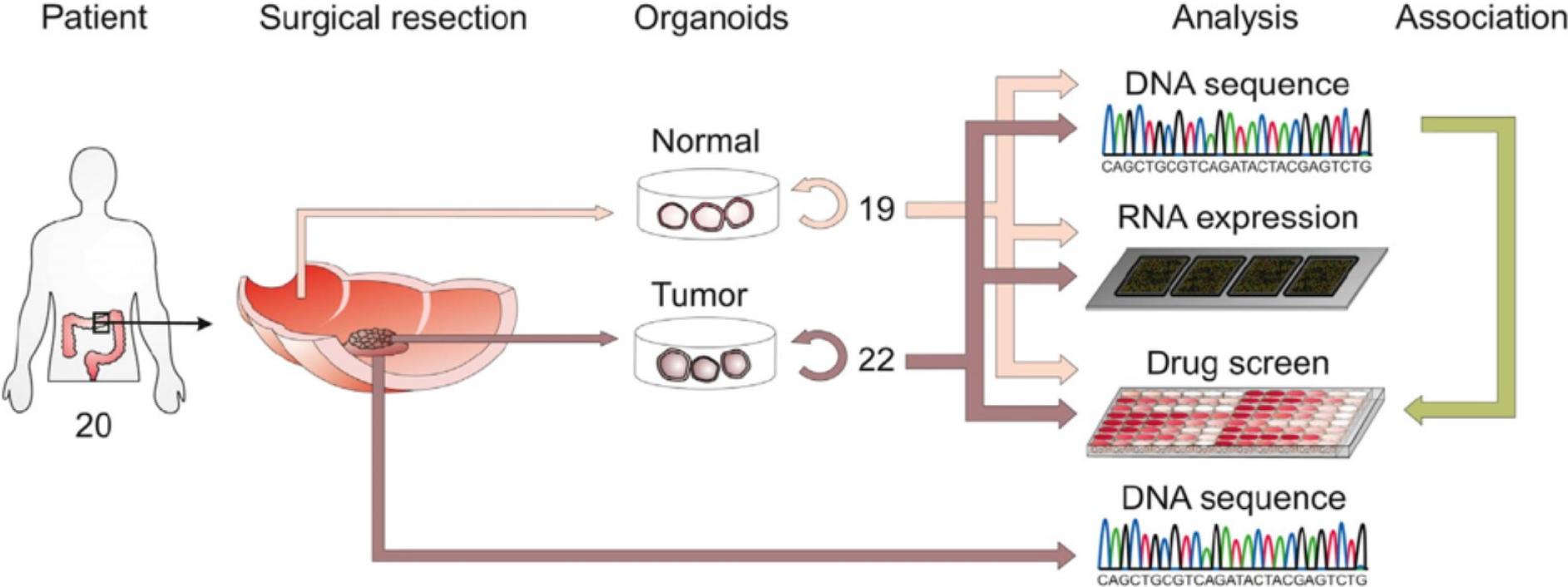


n=187 metastases, 3 mice, $p < 0.002$

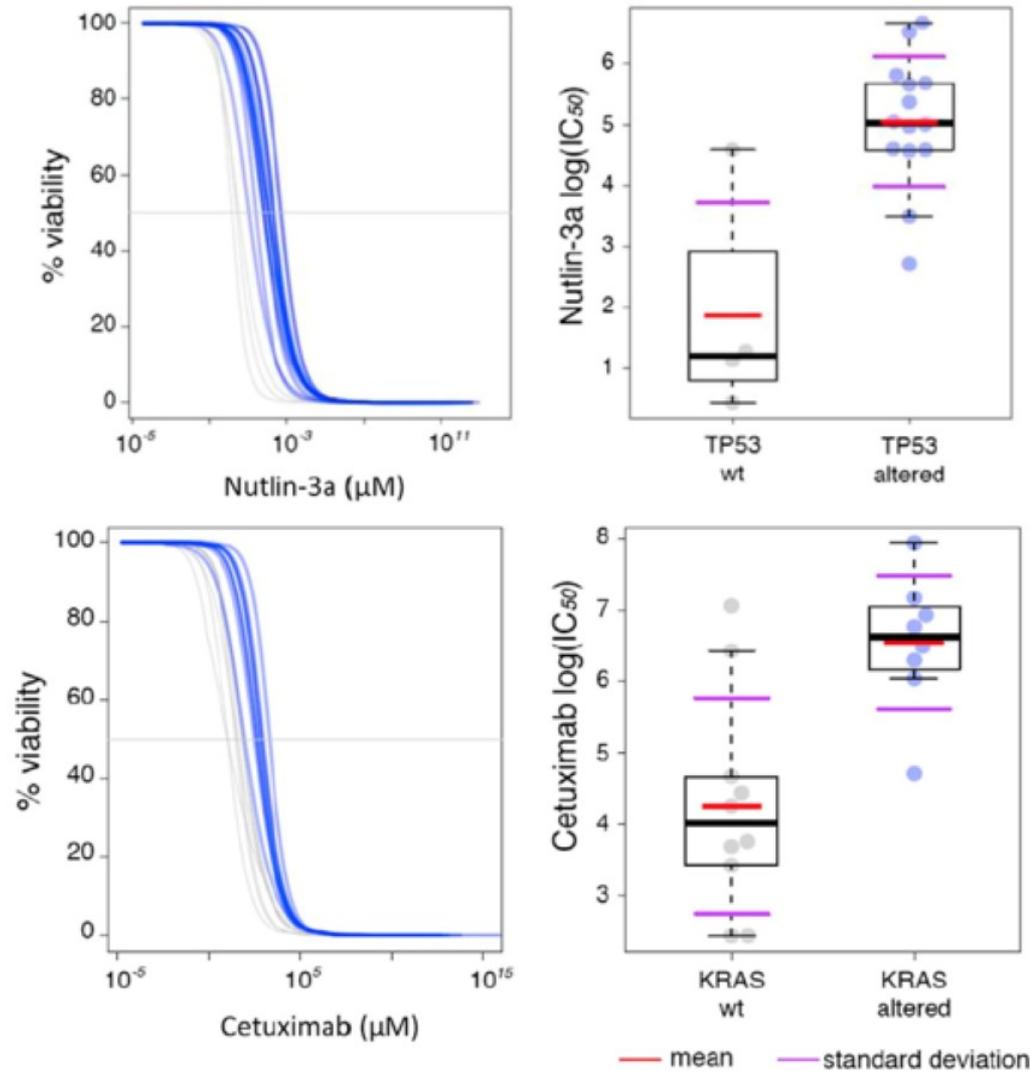
Human Cancer Model Initiative Endpoints

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- **Cancer biology**
 - Models that recapitulate human cancer phenotypes
 - Dependencies on stroma
 - Metastatic propensity
- **Cancer treatment**
 - Models representative of common cancer genotypes/phenotypes that can be used to develop multi-drug combination therapies
 - Models that can predict therapeutic response for an individual patient
 - High-throughput small molecule screening of human cancer models

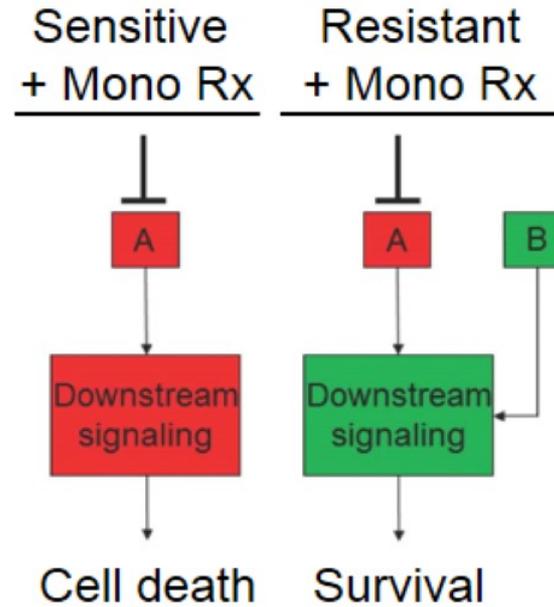
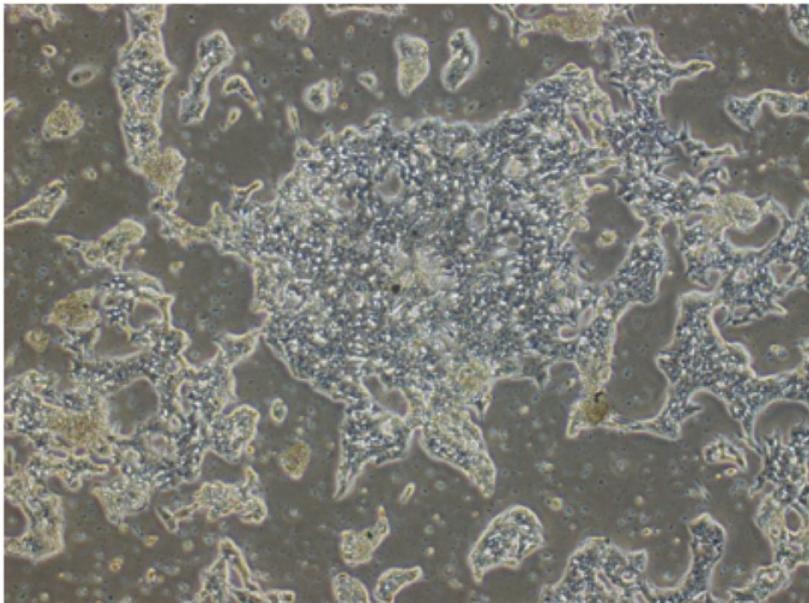
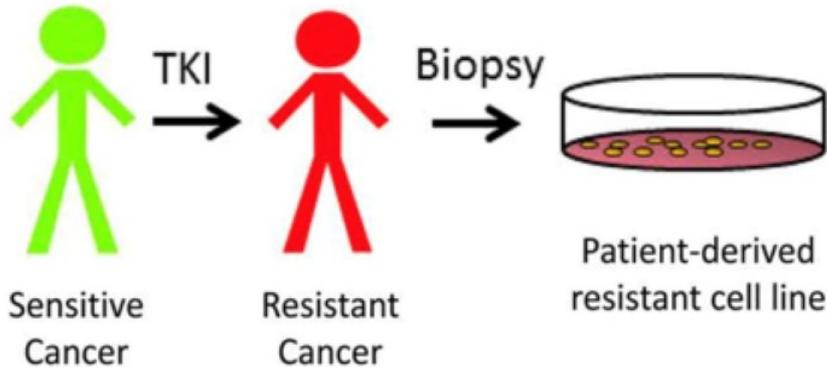
Using Next Generation Cancer Models to Develop Therapies: Colon Cancer Organoids



Using Next Generation Cancer Models to Develop Therapies: Colon Cancer Organoids



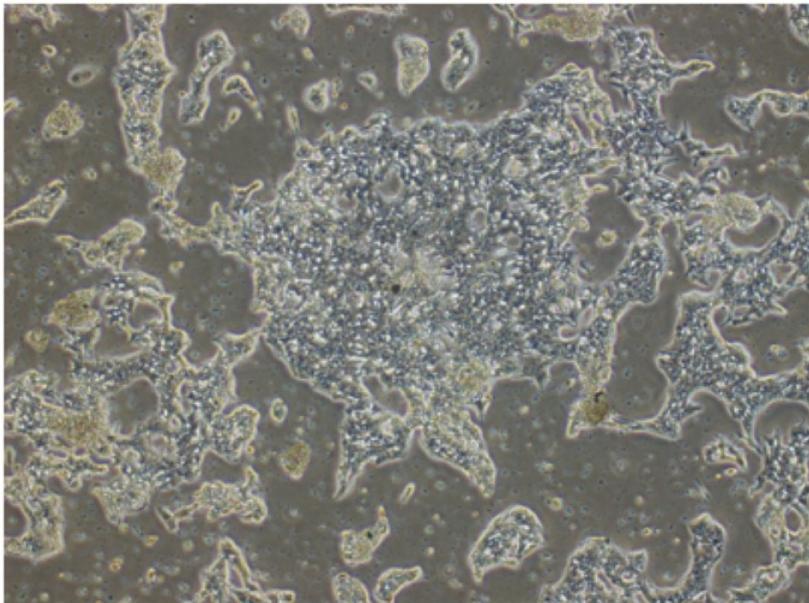
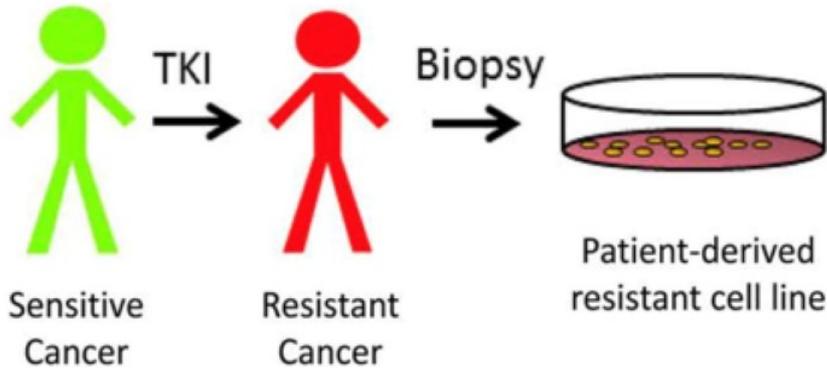
Using Next Generation Cancer Models to Develop Therapies: Lung Adenocarcinoma Conditional Reprogrammed Cells



Engelman laboratory

Crystal et al. Science 2014 346:1480

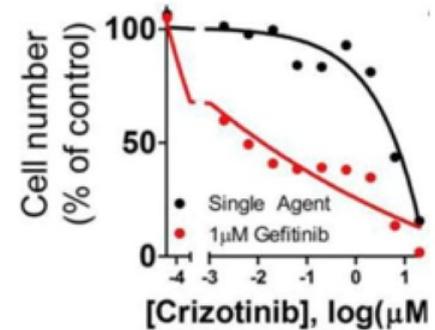
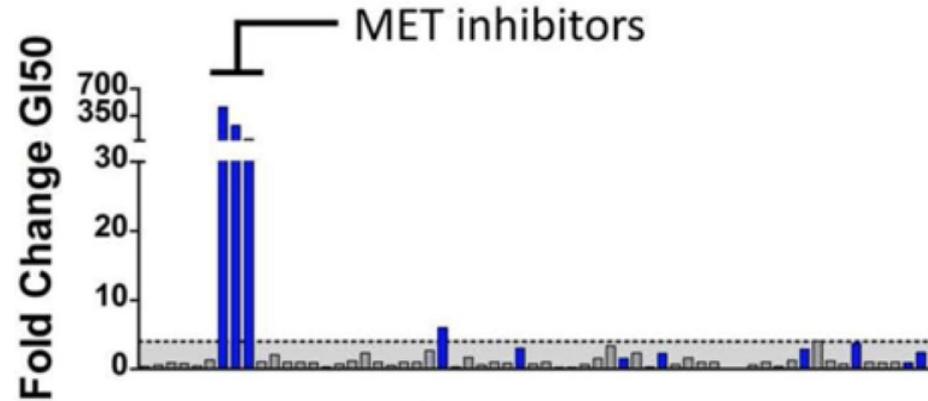
Using Next Generation Cancer Models to Develop Therapies: Lung Adenocarcinoma Conditional Reprogrammed Cells



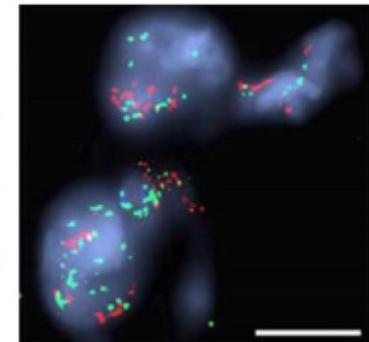
Engelman laboratory

Crystal et al. Science 2014 346:1480

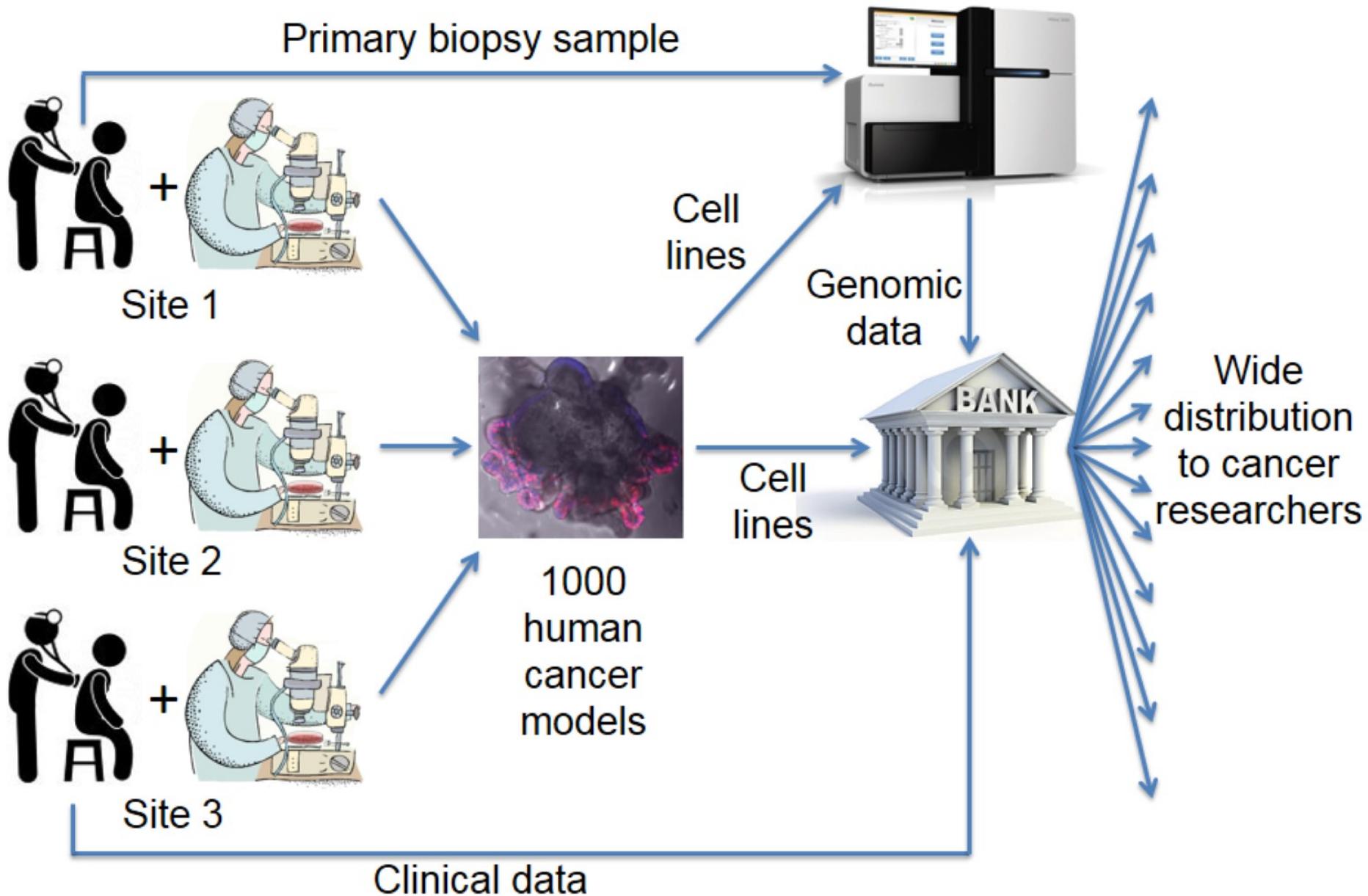
Combo drug screen with Gefitinib



High
level
MET
amp



Human Cancer Model Initiative (HCMI): Pilot Phase



Human Cancer Model Initiative Pilot

Scientific Considerations

- Does the genetic / epigenetic nature of the primary tumor influence its ability to be established or propagated *in vitro*?
- Do the various culture methodologies favor different genetic/epigenetic subpopulations within the primary tumor?
 - Is the subclonal heterogeneity of the primary tumor maintained?
- Can conditions be found to favor growth of malignant epithelium over normal epithelium and vice versa?
 - Is the presence of non-malignant cells a feature or a bug?
- What experimental manipulations are possible?
 - Retroviral/lentiviral transduction? siRNA transfection?
 - CRISPR/Cas9?

Human Cancer Model Initiative Pilot

Methodological Considerations

- Can procedures to establish and propagate models be adopted easily by new laboratories?
 - Are proprietary reagents used that have batch variability?
- Do culture conditions need to be optimized for every organ / tumor type?
- How sensitive are the techniques to variation in surgery / post-surgery handling of tumor?
- Is expansion of cultures limited by time / doublings?
- Does the cellular composition / molecular signature of cultures drift over time?
- Could a third-party distributor provide these cancer models to the research community and ensure reproducibility?

Human Cancer Model Initiative Pilot

Ethical / Regulatory / Procedural Considerations

- Are there barriers to sharing patient cell lines broadly – can privacy and consent issues be handled appropriately?
- Can diagnostic and treatment data be shared?
 - Should the tissue source institution retain a key to patient identity?
- How to adequately protect genomic data from cell lines?
 - What restrictions should apply to cell line resequencing?
- Should drug sensitivity of a patient-derived cancer model be shared with the patient?
 - What would CLIA approval require?
- Are there institutional impediments to sharing methodology and derived cell lines broadly and at an affordable cost?

Human Cancer Model Initiative Pilot Development Plan

- Collaboration established between NCI, Sanger Center (Mike Stratton) and the Hubrecht Institute (Hans Clevers)
 - All three institutions will provide funding and expertise
- Meeting at NCI in July 2015 to discuss operational details
- RFP for contracts to support Human Cancer Model Development Centers in late 2015
- 2 year funding to create ~1000 new human cancer cell lines

Precision Medicine and Cancer Informatics

Warren Kibbe, PhD

NCI Center for Biomedical Informatics

Outline

■ Background

- Attributes require for scalable precision medicine informatics
- How we got here: Lessons from TCGA
- Where we are: Role of the NCI Cancer Genomic Data Commons (GDC) & Cloud Pilots
- Where we are going: Information problems we intend to solve with the Precision Medicine Initiative for Oncology

Some Basic Ingredients for Precision Medicine Big Data

- **Open Science.** Supporting **Open Access, Open Data, Open Source,** and **Data Liquidity** for the cancer community
- **Standardization** through CDEs and Case Report Forms
- **Interoperability** by exposing existing knowledge through **appropriate integration of ontologies, vocabularies and taxonomies**
- **Sustainable models** for informatics infrastructure, services, data, metadata, curation

The Cancer Genome Atlas

A comprehensive effort to accelerate our understanding of the molecular basis of cancer

TCGA: The Cancer Genome Atlas

- Launched in 2006 by NCI & NHGRI
- Complete characterization of ~35 adult cancers
 - ~20 common cancers at 500 cases each
 - ~15 rare cancers at 50-150 cases each
- Copy Number, Gene Expression, Methylation, DNA Sequencing (WGS/WXS), Clinical data
 - ~11,000 cases
- Project ending in 2016
 - Future projects to use the TCGA infrastructure
 - Exceptional Responders, ALChEMIST, Clinical Trial Sequencing Program (CTSP), Cancer Driver Discovery Program (CDDP)
- <http://cancergenome.nih.gov/>



National Cancer Institute

National Human Genome Research Institute



The Cancer Genome Atlas
Data Portal

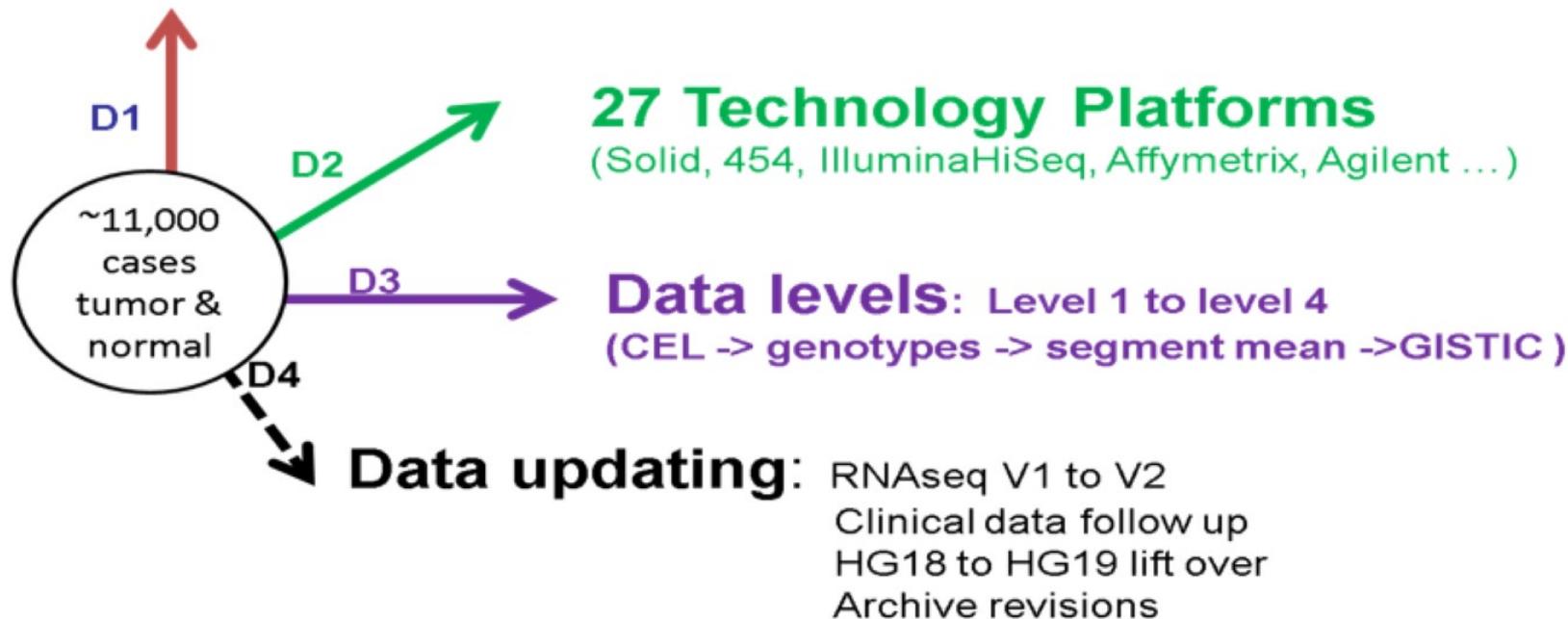


Understanding genomics
to improve cancer care

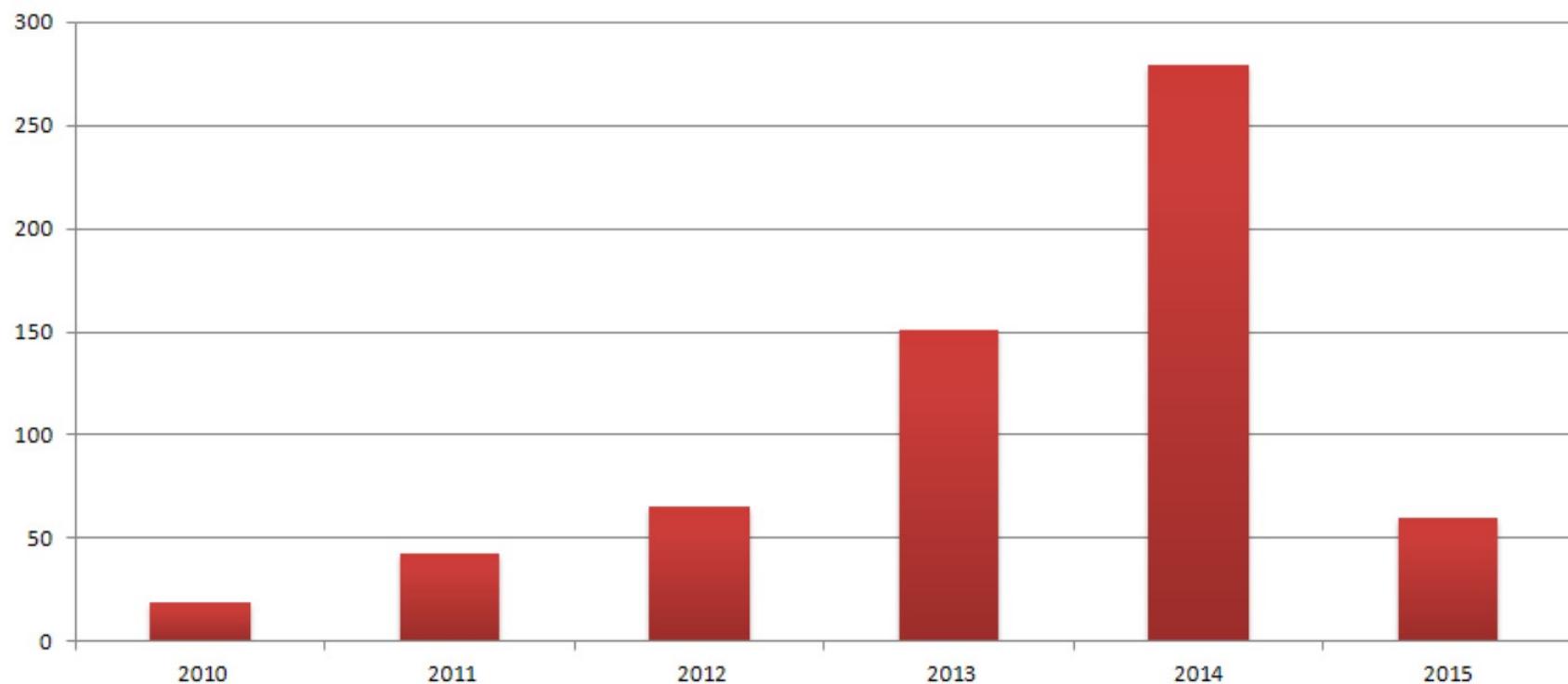
[TCGA Home](#) | [Contact Us](#) | [For the Media](#)

Dimensions of TCGA Data

12 Data types: Expression, Methylation, DNaseq, RNAseq ...



TCGA Publications since 2010



Cancer study reveals powerful new system for classifying tumors

One in ten cancers were reclassified in clinically meaningful ways based on molecular subtypes identified by a comprehensive analysis of data from thousands of patients

August 07, 2014

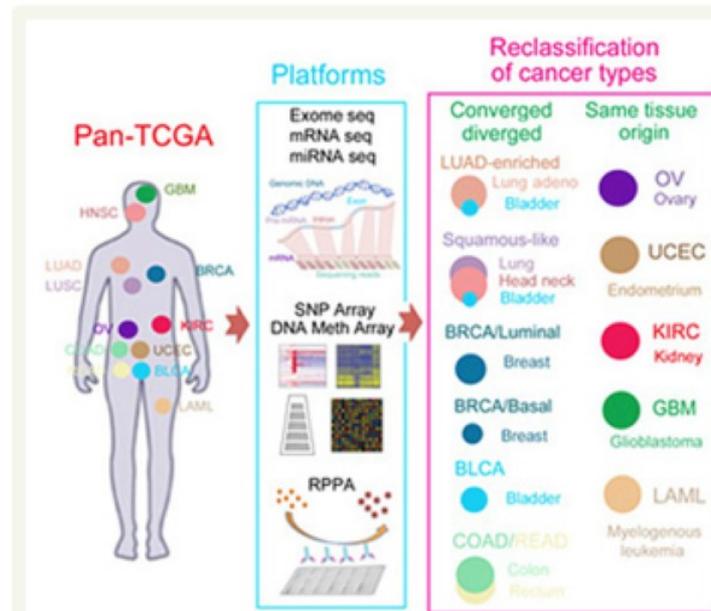
By [Tim Stephens](#)

SHARE THIS STORY: [t](#) [f](#) [g+](#) [in](#) [v](#)

Example publication from TCGA

Cancers are classified primarily on the basis of where in the body the disease originates, as in lung cancer or breast cancer. According to a new study, however, one in ten cancer patients would be classified differently using a new classification system based on molecular subtypes instead of the current tissue-of-origin system. This reclassification could lead to different therapeutic options for those patients, scientists reported in a paper published August 7 in *Cell*.

"It's only ten percent that were classified differently, but it matters a lot if you're one of those patients,"



The Genomic Data Commons

Facilitating the identification of molecular subtypes of cancer and potential drug targets

NCI Cancer Genomic Data Commons (GDC)



Genomic Data Commons (GDC) – Rationale

- TCGA and many other NCI funded cancer genomics projects each currently have their own DCC
 - BAM data and results stored in many different repositories; confusing to users, inefficient, barrier to research
- GDC will be a single repository for all NCI cancer genomics data
 - Will include new, upcoming NCI cancer genomics efforts
 - Store all data including BAMs
 - Harmonize the data as appropriate
 - Realignment to newest human genome standard
 - Recall all variants using a standard calling method
 - Will be the authoritative reference data set

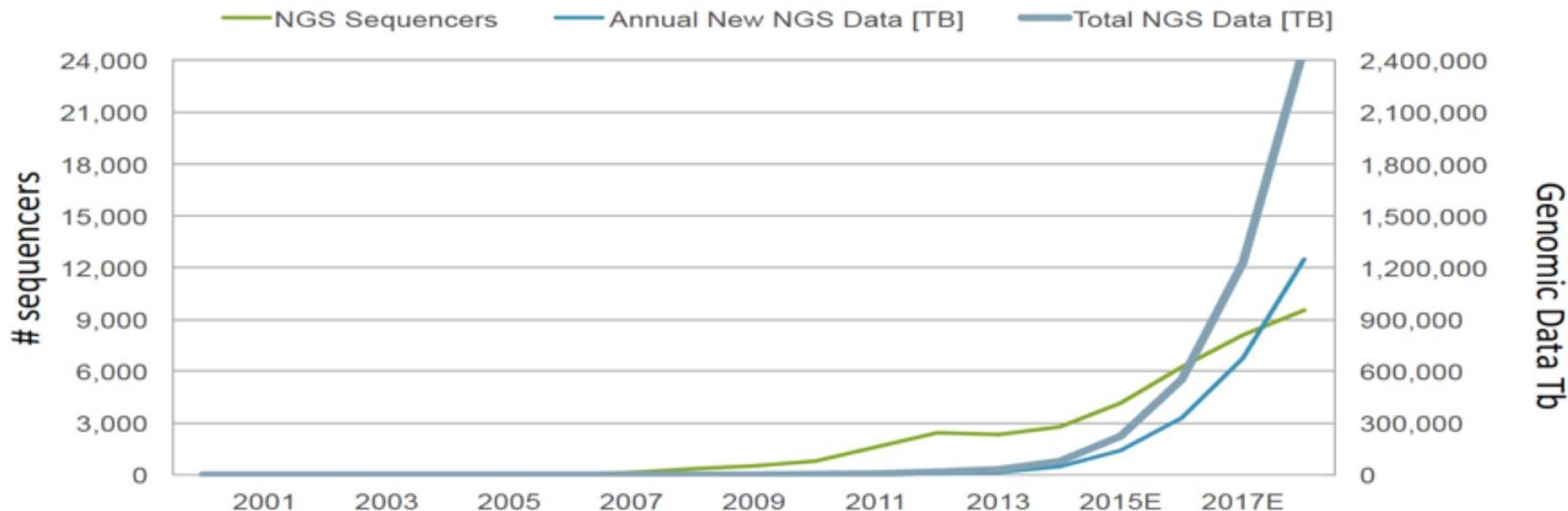
Genomic Data Commons (GDC)

- First step towards development of a knowledge system for cancer
- Foundation for a genomic precision medicine platform
- Project initiated Spring of 2014
 - Contract awarded to University of Chicago
 - PI: Dr. Robert Grossman
 - Go live date: Late Spring 2016
 - Not a commercial cloud
- Data will be freely available for download subject to data access requirements

The NCI Cancer Genomics Cloud Pilots

*Understanding how to meet the research
community's need to analyze large-scale cancer
genomic and clinical data*

Amount of genomic data will exceed available resources



Between 2014-2018 production of new NGS data to exceed **2 Exabytes**

NGS: Next Generation Sequencing

NGS sequencers include machines from Illumina, Life Technologies, and Pacific Biosciences. Human genome data based on estimates of whole human genomes sequenced

Sources: Financial reports of Illumina, Life Technologies, Pacific Biosciences; revenue guidances; JP Morgan; The Economist; Seven Bridges Analysis.

NCI Cloud Pilots

The Broad

PI: Gad Getz

Institute for Systems Biology

PI: Ilya Shmulevich

Seven Bridges Genomics

PI: Deniz Kural

Period of performance:

Sept 2014 – Sept 2016



NCI GDC and the Cloud Pilots

- Working together to build **common APIs**
- Working with the Global Alliance for Genomics and Health (**GA4GH**) to **define** the next generation of **secure, flexible, meaningful, interoperable, lightweight interfaces**
- Competing on the **implementation**, collaborating on the **interface**
- Aligned with **BD2K** and serving as a part of the **NIH Commons** and working toward shared goals of **FAIR** (Findable, Accessible, Interoperable, Reusable)
- Exploring and defining **sustainable precision medicine information infrastructure**

Information problem(s) we intend to solve with the Precision Medicine Initiative for Oncology

- **Establish** a sustainable infrastructure for cancer genomic data – through the **GDC**
- **Provide** a data integration platform to allow multiple data types, multi-scalar data, temporal data from cancer models and patients
 - Under evaluation, but it is likely to include the GDC, TCIA, Cloud Pilots, tools from the ITCR program, and activities underway at the Global Alliance for Genomics and Health
- **Support** precision medicine-focused clinical research

NCI Precision Medicine Informatics Activities

- As we receive additional funding for Precision Medicine, we plan to:
 - **Expand** the GDC to handle additional data types
 - **Include** the learning from the Cloud Pilots into the GDC
 - **Scale** the GDC from 10PB to hundreds of petabytes
 - Include imaging by interoperating between the GDC and the **Quantitative Imaging Network TCIA** repository
 - **Expand** clinical trials tooling from NCI-MATCH to NCI-MATCH Plus
 - **Strengthen** the ITCR grant program to explicitly include precision medicine-relevant proposals

Bridging Cancer Research and Cancer Care

- Making clinical research relevant in the clinic
- Supporting the virtuous cycle of clinical research informing care, and back again
- Providing decision support tools for precision medicine

But how?

Precision Medicine informatics community engagement

- Ongoing

- Cancer Informatics for Cancer Centers Clinical Genomics Workshops (Nov '13, May '14, Nov '14, March '15) <http://ci4cc.org>
- Global Alliance for Genomics and Health Data and Clinical Working Groups (March '14, Oct '14, June '15) <http://genomicsandhealth.org/>

- Planned

- Convene a community informatics workshop Fall/Winter 2015

Thank you



Warren Kibbe
warren.kibbe@nih.gov

Thanks to content contributors:

Sherri de Coronado, Gilberto Fragoso, Mark Jensen, Warren Kibbe, Juli Klemm, Tony Kerlavage, JC Zenklusen, Elizabeth Gillanders and others.



**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol

Cancer Genomics Project Teams

CGC Pilot Team Principal Investigators

- **Gad Getz, Ph.D** - Broad Institute - <http://firecloud.org>
- **Ilya Shmulevich, Ph.D** - ISB - <http://cgc.systemsbiology.net/>
- **Deniz Kural, Ph.D** - Seven Bridges – <http://www.cancergenomicscloud.org>

NCI Project Officer & CORs

- Anthony Kerlavage, Ph.D –Project Officer
- Juli Klemm, Ph.D – COR, Broad Institute
- Tanja Davidsen, Ph.D – COR, Institute for Systems Biology
- Ishwar Chandramouliswaran, MS, MBA – COR, Seven Bridges Genomics

GDC Principal Investigator

- Robert Grossman, Ph.D - University of Chicago

Center for Cancer Genomics Partners

- JC Zenklusen, Ph.D
- Daniela Gerhard, Ph.D
- Zhining Wang, Ph.D
- Liming Yang, Ph.D
- Martin Ferguson, Ph.D

NCI Leadership Team

- Warren Kibbe, Ph.D
- Lou Staudt, M.D.
- Steven Chanock, Ph. D
- George Komatsoulis, Ph.D

Non-Communicable Disease Regional Infrastructure Core Planning Grants

Edward L. Trimble, MD, MPH

Director

Center for Global Health

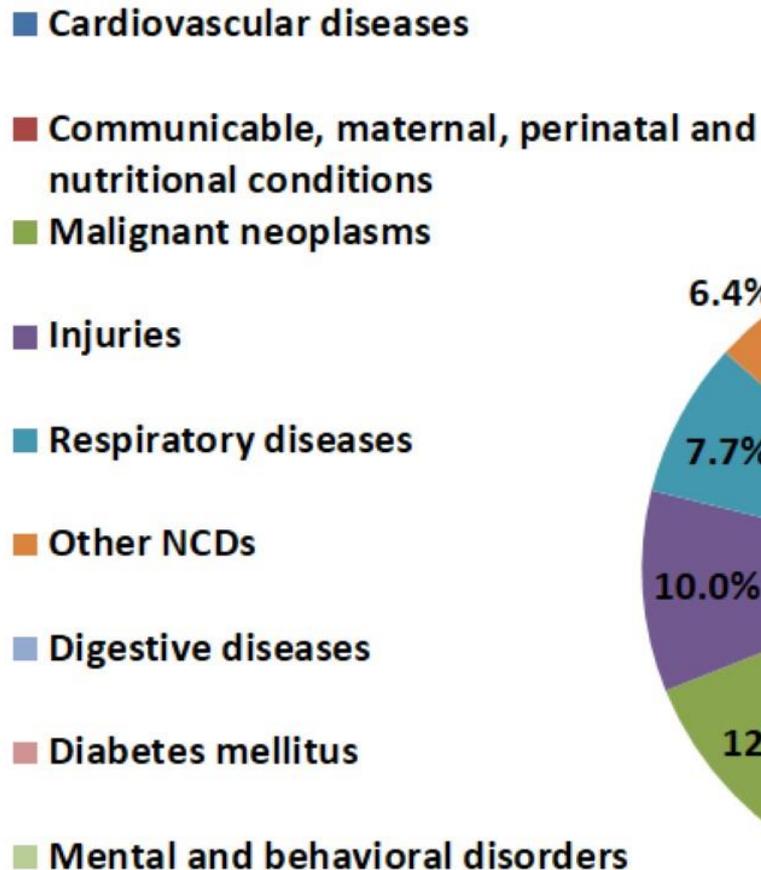
National Cancer Institute

National Institutes of Health

Concept Summary

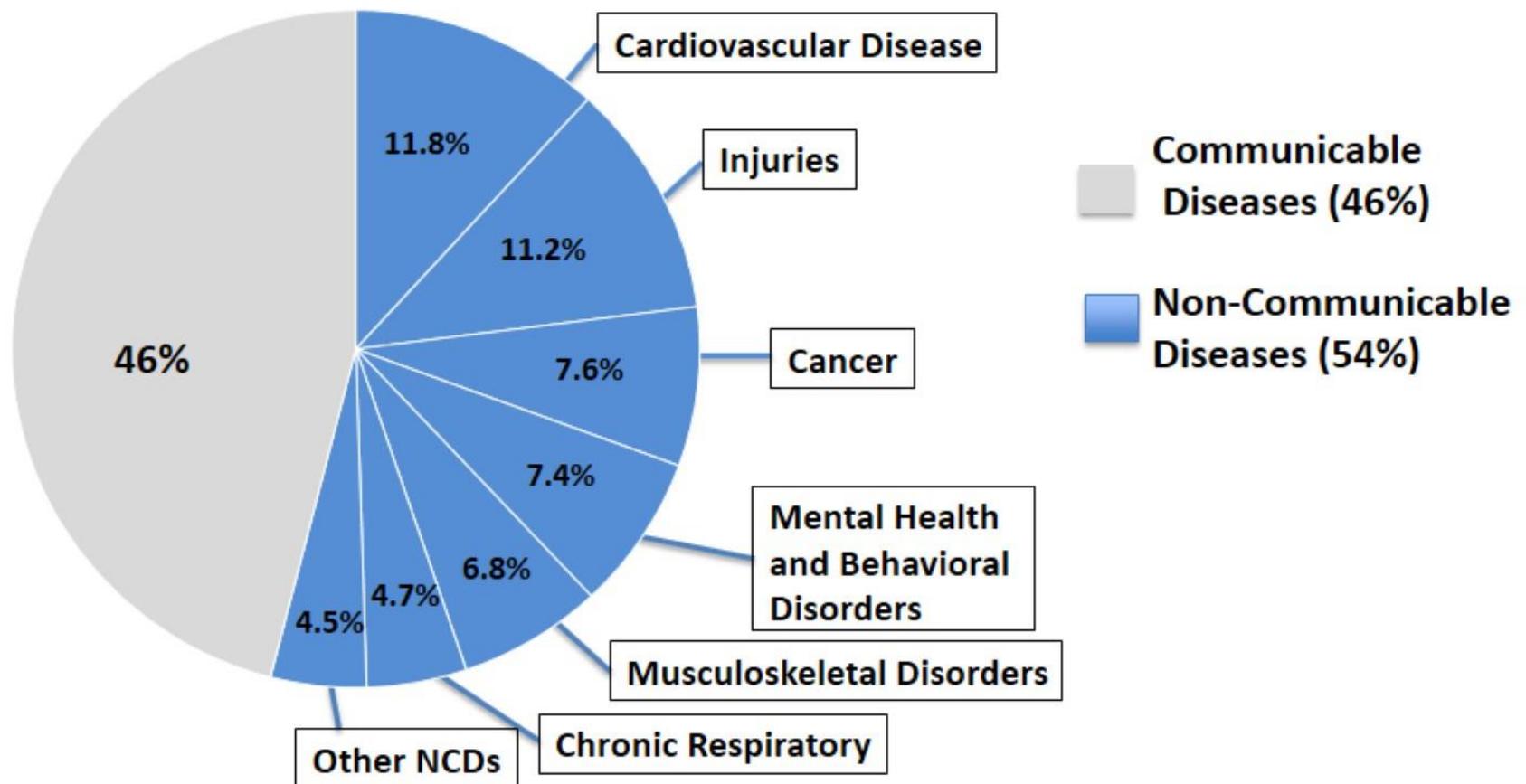
To support activities for the planning and design of sustainable, regional research infrastructure core (RICs), established to build, strengthen, and coordinate research and training of non-communicable diseases (NCDs) in low- and middle-income countries (LMICs) or regions.

NCDs and Injury in LMICs



More than 70% of premature deaths in LMICs are caused by NCDs and injury

DALYs for Communicable Diseases vs. Non-Communicable Diseases



NCDs Have Common Risk Factors

1. Tobacco use
2. Physical inactivity
3. Unhealthy diet
4. Harmful use of alcohol
5. Environmental factors
 - a. Outdoor air pollution
 - b. Indoor air pollution



Current Challenges to Addressing NCDs in LMICs

1. Limited in-country financial support for research and training
2. Inadequate research infrastructure
3. Poor healthcare delivery services, limiting the ability to conduct clinical research
4. Lack of surveillance regarding the management of NCDs
5. Lack of coordination across activities for addressing NCDs at country and regional-levels

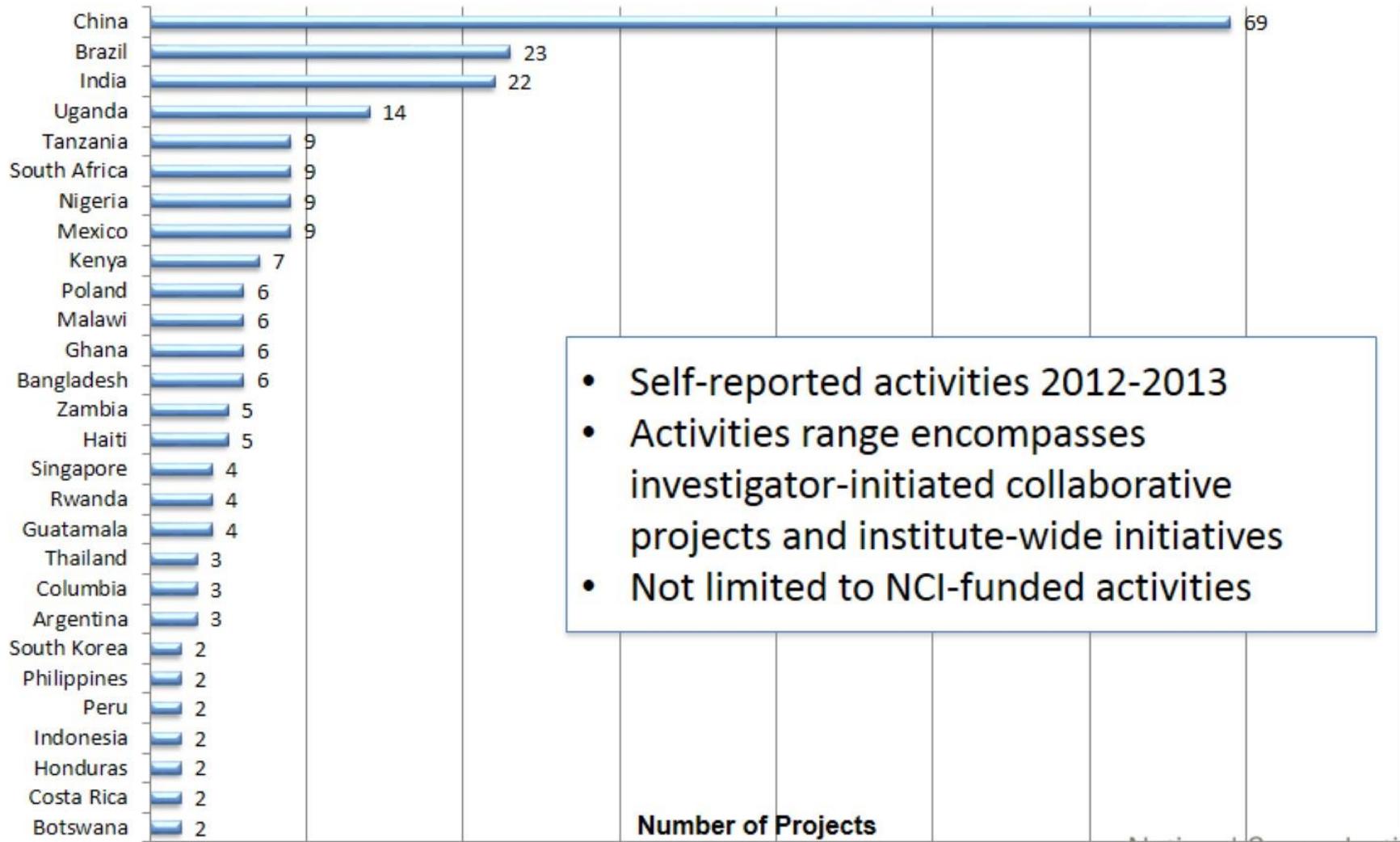
Leverage Existing USG and Other Infrastructure

1. **PEPFAR** *President's Emergency Plan for AIDS Relief*
2. **NIAID** *Clinical Trial Units for NIAID Networks*
3. **NHLBI** *Centers of Excellence*
4. **NICHD** *Biomedical/Biobehavioral Research Administration Development (BRAD) Award*
5. **NIMH** *Collaborative Hubs for International Research in Mental Health*
6. **FIC** *Medical Education Partnership Initiative (MEPI)*
7. **NHGRI** *H3 Africa – Human heredity and health in Africa*

Leverage Existing USG and Other Infrastructure

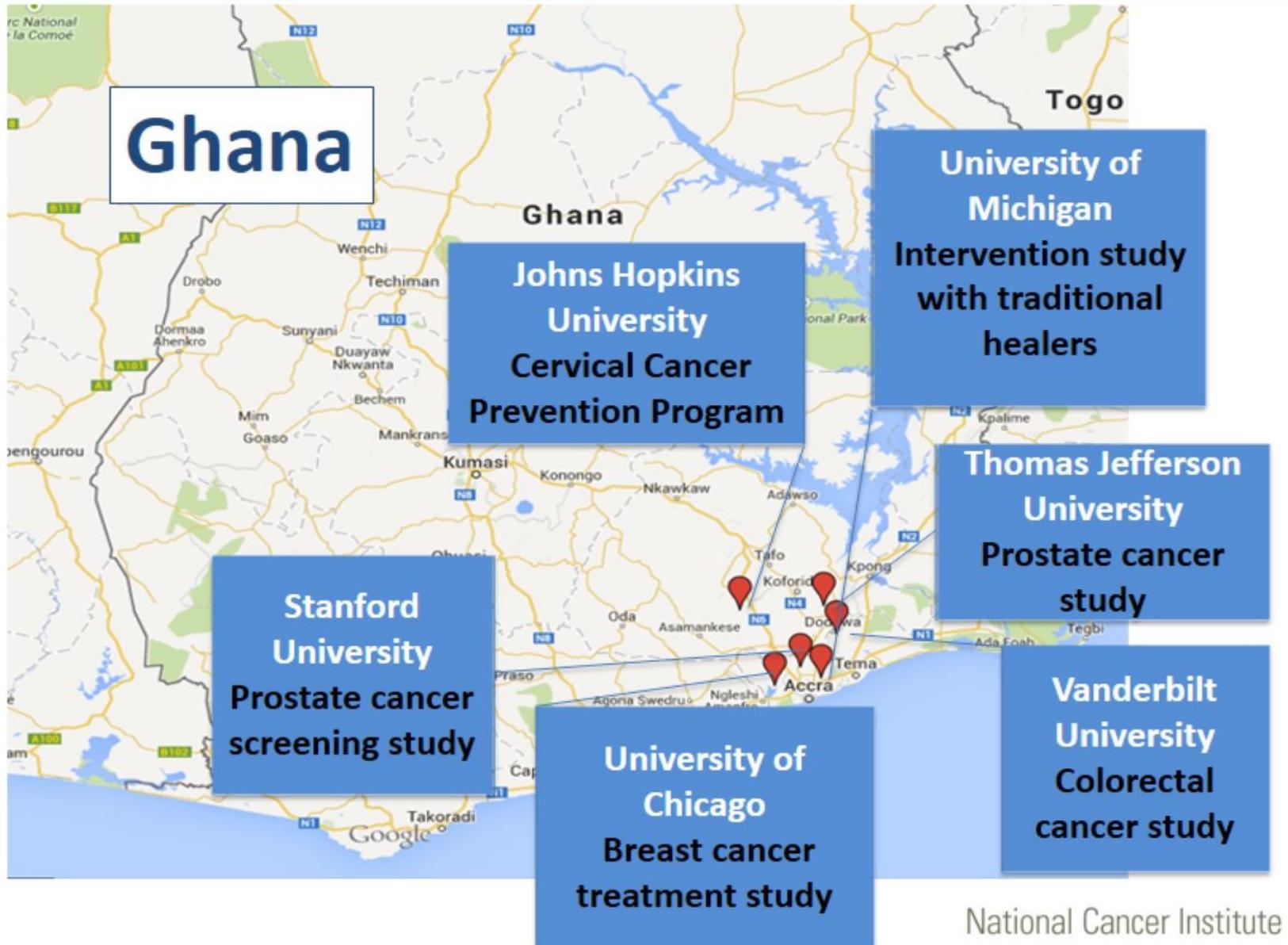
1. **OAR-NIAID-NCI, et al.** *Centers for AIDS Research (CFAR)*
2. **NCI-OHAM** *Strengthening Capacity for Research on HIV-associated malignancies in Africa*
3. **FIC-NCI-NHLBI** *TOBAC partnerships for tobacco control research*
4. **FIC-NIH ICs** *GEOHealth Network*
5. **CDC** *Field Epidemiology Training Programs*

International Activities of NCI Designated Cancer Centers



- Self-reported activities 2012-2013
- Activities range encompasses investigator-initiated collaborative projects and institute-wide initiatives
- Not limited to NCI-funded activities

Number of Projects



UK Universities Working in Ghana

1. University of Bristol
2. University of Cambridge
3. University of London,
Imperial College
4. University of Glasgow
5. University of Manchester
6. University of Reading
7. University of Oxford
8. University of Southampton
9. University of Surrey
10. Barts Cancer Institute
11. Institute for Cancer
Research, London
12. Kings College, London
13. Leeds
14. NICE
15. Queens University, Belfast
16. Royal Marsden Hospital
17. University College, London
18. University of Warwick

AMPATH Model

Founders:

- **Goal:** To create a sustainable research program including Research Program Office; Research and Sponsored Programs; Institutional Review Board; and ISO certified laboratory
- **Overarching Principle:** Each Research Project must have both a North American and a Kenyan principal investigator
- **Established:** In 1998; based in El Doret, Kenya



*Indiana University, Moi University SOM
Moi Teaching & Referral Hospital*

AMPATH Model

- 1. Current Leadership:** Dr. Rachel Vreeman, Indiana University and Dr. Winstone Nyandiko, Moi University
- 2. Kenya Partners:** Moi University School of Medicine and Moi Teaching and Referral Hospital
- 3. USG Partner:** USAID-PEPFAR and five NCI-designated Cancer Centers
- 4. North American Partners:** Indiana Univ., Brown Univ., Duke Univ., Lehigh Valley Hospital, Provident Portland Medical Center, Purdue Univ., Univ. of Massachusetts, Univ. of Toronto, and Univ. of Utah

AMPATH Program Structure

- **5 Co-Field Directors for Research**

 - 3 are full-time in Kenya

- **9 Research Working Groups**

 - Adult medicine, Basic science, Behavioral & social science, Cardiovascular and pulmonary disease, Oncology, Pediatrics, Public health & primary care, Reproductive health, and Tuberculosis

- **7 Core Facilities**

 - Operations, Data management, Biostatistics, Clinical informatics, Pharmacy, Laboratory, and Bioethics

AMPATH Outcomes, 17 Years Later

1. Over 90 active research projects
2. More than \$83.4M in research funding
3. Collaborators from > 19 universities and academic institutions in Africa, Europe, and North America
4. More than 275 publications

Long-Term Goals of NCD RICs:

1. Strengthen commitment of LMIC countries to public health research and implementation
2. Build evidence base for NCD prevention and control in LMICs
3. Build global health career track for investigators focused on NCDs
4. Facilitate individual research projects through use of Regional Research Cores
5. Strengthen multidisciplinary research across NCDs

Specific Activities of the Planning Grants

1. Assess NCD research needs and opportunities in the region of interest
2. Encourage the coalescence of a consortium of universities/cancer centers willing to work together in a region or country
3. Plan coordination of:
 - a. Research projects
 - b. Infrastructure core development
 - c. Research training
4. Develop strong application for core funding

Characteristics of a NCD Regional Infrastructure Core (RIC)

1. Partnership between a consortium of US/HIC institutions and multiple LMIC institutions in specific country or region
2. Development of research core facilities
3. Training and career development
 - a. US/HIC countries: global health research career track
 - b. LMIC countries: cancer and NCD research
4. Research to policy
 - a. Links between research community, government, and civil society
 - b. Address critical cancer & NCD public health issues
 - c. Use evidence to guide public policy and clinical practice

Potential NIH Partners:

1. Fogarty International Center
2. NHLBI (similar proposal in internal review)
3. NICHD
4. NIDDK
5. NIGMS (surgery & injury)
6. NIMH
7. NINDS
8. NINR
9. Etc.

Potential Research Areas

- Epidemiology and risk factor modification
- Genetics, genomics, and epigenetics
- Molecular and cellular biology
- Implementation science and knowledge sharing
- Health disparities/ social determinants of health
- Prevention and health surveillance
- Behavioral science
- Detection, diagnosis, and treatment
- Symptom management & survivorship
- Informatics/ UPIN/ data linking
- Health surveillance, including cancer registries, death registries, HBV & HPV vaccination, cancer risk factors
- mHealth, eHealth

Potential Core Resources

1. Grants & contracts management
2. Research ethics oversight (IRBs)
3. Bioinformatics & data management
4. Biostatistics
5. Biobanking
6. Health communications
7. Health economics/ comparative effectiveness research

Evaluation Criteria for the Planning Grants

1. Quality of the comprehensive needs assessment of NCD-related research needs for the region
2. Caliber of the research plan to support NCD research needs of the region
3. Training plan aligned with the proposed NCD research
4. Appropriate infrastructure cores to support NCD research
5. In-depth metrics for monitoring and evaluating the quality and scientific impact of the research, training, and infrastructure

Evaluation Criteria of the Planning Grants, con't.

6. Strong, authentic community engagement to identify and addresses the local research needs
7. Strengthened administrative capacity of the LMIC institution to support the research
8. Credible plan for building self-sustaining, internationally-competitive research program

Network of NCD Consortia

1. Learning network
 - Can share best practices and lessons learned
2. Central NIH coordination
 - Similar to NCI Provocative Questions model

Potential HIC and UMIC Country Partners

High-income countries

- Australia (focus on SE Asia)
- Canada
- France
- Germany
- Ireland
- Japan
- Korea
- Norway

Upper middle-income countries

- Brazil (Portuguese-speaking countries)
- China
- India
- South Africa

Potential RIC Locations



Mechanism and Funds Available

1. RFA – P20
2. NCI expects to make 6, 2-year, \$200,000 dollar direct cost awards (\$330K, total costs)
 - a. Other ICs may make additional awards or co-sponsor awards
3. \$2.4 million dollars, direct costs (\$4M total costs)
 - a. \$1.2 million dollars, direct costs, in each FY16 and FY17

Thank You

CGH

John Flanigan
Shannon Silkensen

DCP

Brandy Heckman-Stoddard
Ann O'Mara
Heng Xie

OCC

Hasnaa Shafik

DCCPS

Brenda Edwards
Damali Martin

DCTD

Miguel Ossandon

OHAM

Kishor Bhatia
Geraldina Dominguez

CCT

Susan Perkins

Funded Projects

Cancer Center	Title	Principal Investigator
University of Texas M.D. Anderson	A Low Cost Optical Imaging Tool for Cervical Cancer Prevention	Dr. Kathleen Schmeler
Virginia Commonwealth University - Massey	Cloud-based Collaboration for Radiotherapy Clinical Trials, Research and Training.	Dr. Jatinder Palta
Dana Farber	Tobacco-Free Teachers: Pilot study to assess program adoption in schools in India	Dr. Glorian Sorenson
Melvin and Bren Simon	Vincristine Optimization in Kenyan Children with Cancer	Dr. Jodi Skiles
Vanderbilt-Ingram	Cancer Bioinformatics Network in the Central America LMICs: Gastric Cancer Focus	Dr. Jennifer Pietenpol
Johns Hopkins-Sidney Kimmel	HIV Infection, Viral Hepatitis, Hepatocellular Carcinoma in Uganda	Dr. Gregory Kirk
Memorial Sloan-Kettering	Expanding a team of clinical investigators in Nigeria with a prospective colorectal cancer biobank and database.	Dr. T. Peter Kingham
UCSF-Helen Diller	A Study of Etiology of Esophageal Cancer in Tanzania	Dr. Robert Hiatt, Dr. Katherine Van Loon

Funded Projects (cont.)

Cancer Center	Title	Principal Investigator
Norris Cotton	Tanzanian Research Training Program in HIV Related Malignancies	Dr. Mark S. Ernstoff
University of Wisconsin-Carbone	An African Pain Policy Fellowship: a Pilot Regional Collaboration to Improve Opioid Availability for Cancer Pain	Dr. James Cleary
St Jude	St. Jude Comprehensive Cancer Center -Pequeno Principe Research Institute Twinning Program	Dr. Gerard Zambetti
University of North Carolina-Lineberger	Building Cooperation & Capacity for Cervical Cancer Research between LCCC, Zambia & Malawi	Dr. H. Shelton Earp
Fred Hutchinson	Expanding Capacity for Infection-Related Cancer Research by Examining the Contribution of Viral Genomic Diversity to the Clinical Manifestations of Cancer in Uganda	Dr. Corey Casper Dr. Alena Anderson
Roswell Park	Initiative to Improve Cancer Care in Ghana and Nigeria	Dr. Alex Adjei
UCSD-Moores	Training Chilean Bioinformatics Researchers in the Cancer Genomics Field	Dr. Anil Sadarangani Dr. Catriona Jamieson

Clinical Proteomic Tumor Analysis Consortium

RFA renewal

Henry Rodriguez
June 24, 2015

- **Part 1: What we've learned**
 - What was CPTAC funded to do?
 - What has CPTAC accomplished in 3.5 years?
- **Part 2: What might be next**
 - Proposed concept (overarching goals)
 - Structure, mechanisms and budget

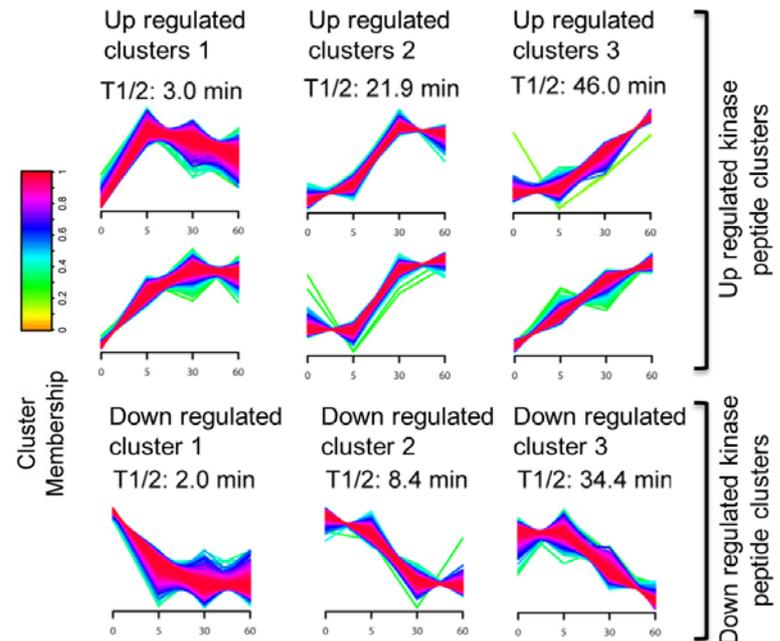
Part 1: CPTAC program current scope

- What was CPTAC funded to do?
 - Goal: Elucidate the proteogenomic complexity of tumors by identifying proteins that derive from alterations in cancer genomes [TCGA tumors: colorectal cancer (CRC), ovarian cancer (OVC), breast cancer (BRC)]
 - Underlying question: Would additional biology be elucidated from deep proteomic analysis [CPTAC1] on genomically characterized tumors [TCGA]?
- Achieved through...
 - Proteome Characterization Centers - consortium of five labs that coordinate standardized research activities
 - Sample size (CRC - 95; OVC - 174; BRC - 105)
 - Community resources (data, assays, reagents)

Challenges overcome in Year 1

- Retrospective biospecimens (samples of convenience)
 - **Scientific implication:** effects of pre-analytical variables associated with TCGA tumors on protein measurement
 - Cold ischemia (up to 60 min)
 - **Good news:** no significant change in protein levels; change in phosphorylation levels, but biologically coherent
 - **Programmatic impact:**
 - Proteomic analysis of **TCGA samples not until Year 2**
 - **Good news:** ischemic proteomic database; prospective collection (tissue); SOPs/Best Practices to be adopted by College of American Pathologists

Temporal dynamics of phosphorylation changes resulting from cold ischemia during surgical procedures.



Colorectal Cancer: global protein abundance (proteome subtypes identified)



Transcriptome Subtypes

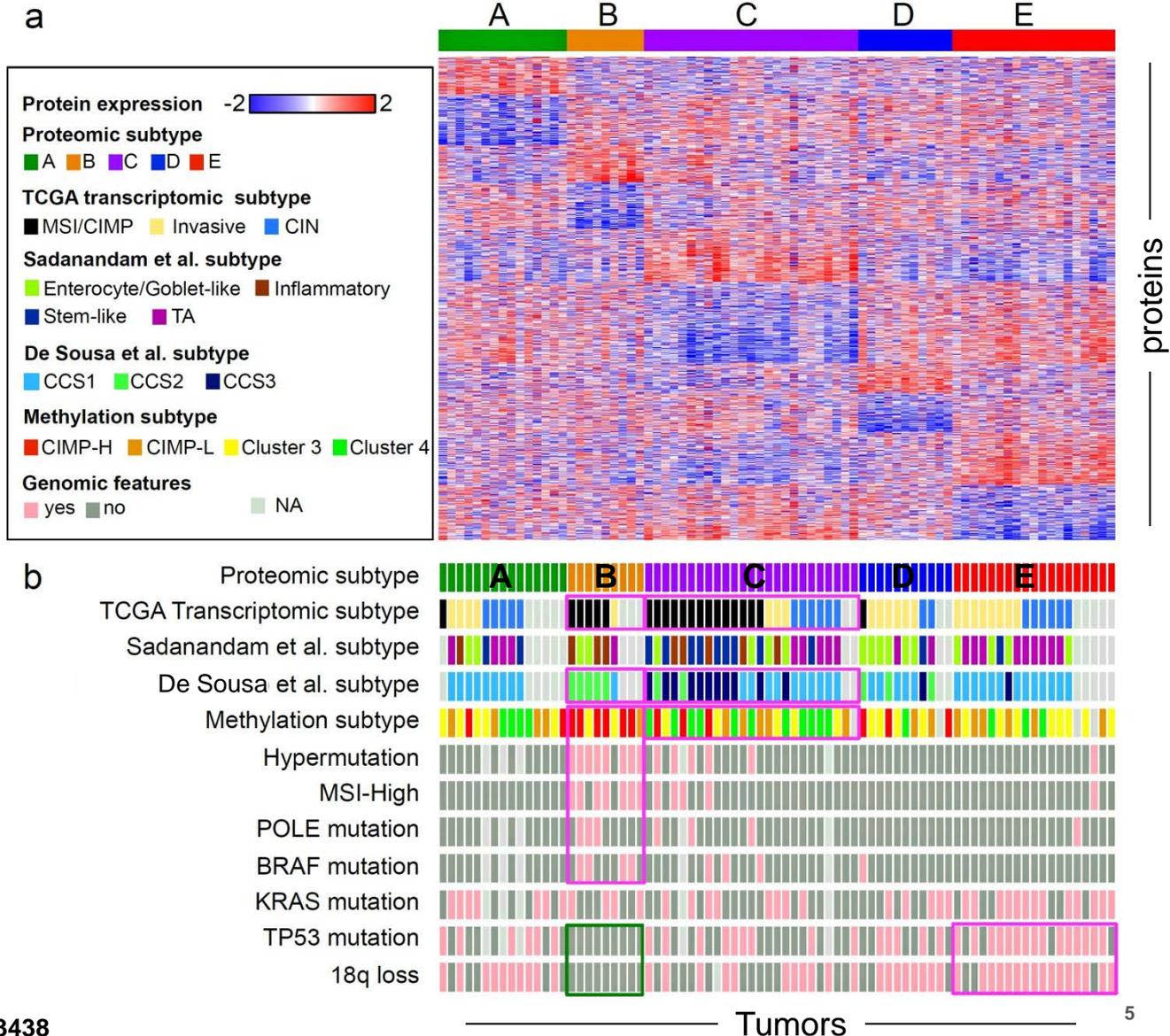
- MSI/CIMP
- Invasive
- CIN



Proteome Subtypes

- A
- B
- C
- D
- E

- MSI/CIMP transcriptome subtype split into two proteome subtypes
- Subtype C displayed protein network features characteristic of EMT, associated with rapid metastasis and overall poor survival





Next steps (e.g.):

- **Q1. Can we rediscover the proteome subtypes?**
 - Global analysis on independent collection (CPTAC prospective samples: 100 treatment-naïve tumors and normal)
- **Q2. Can targeted proteomic assay panels identify interesting proteome features?**
 - *Proteome Subtype Panel*: 80 proteins representing the five CRC subtypes (CPTAC prospective)
- **Q3. Can targeted proteomic assay panels identify clinically relevant features?**
 - *Proteome Subtype Panel*: evaluate ability to discriminate recurrent from non-recurrent tumors (GI SPORE: 64 treatment-naïve tumors)

Ovarian Cancer: global protein abundance (proteome subtypes identified)

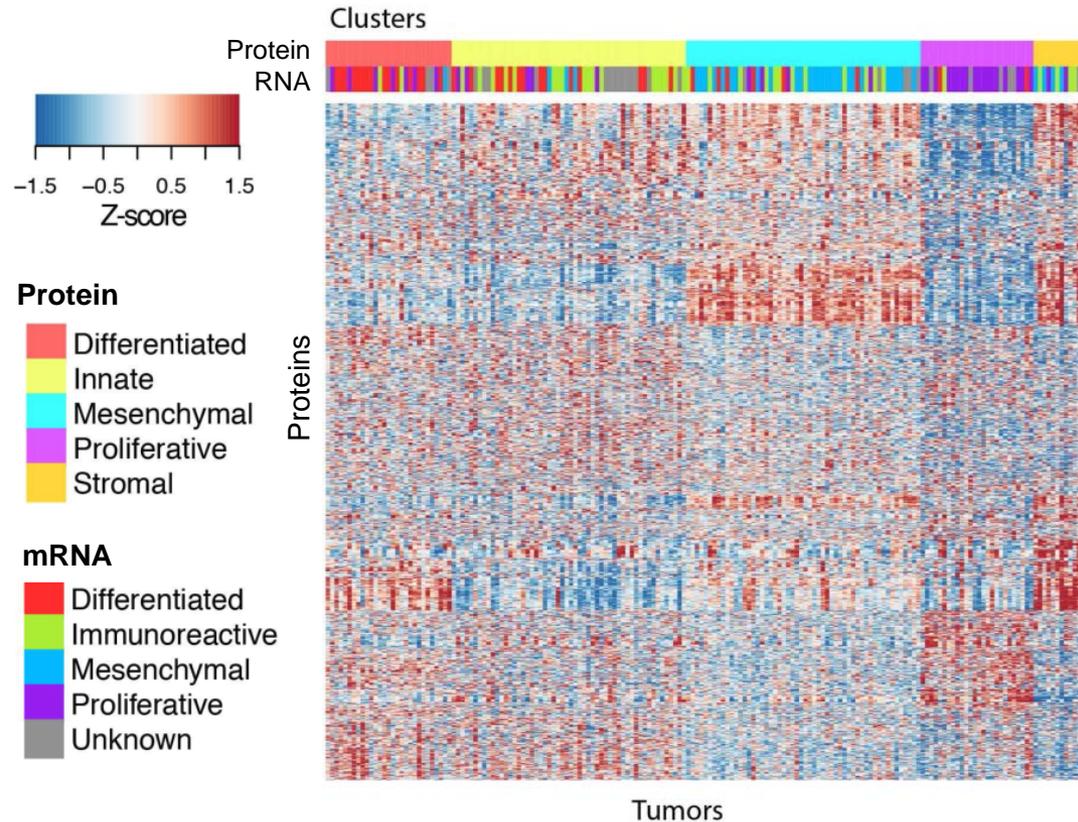


- **174 ovarian HGSC tumors**

- Selection criteria:
 - Overall Survival (OS)
 - Homologous Recombination Deficiency status (HRD)

- **5 proteomic subtypes**
(4 transcriptomic subtypes)

- Immunoreactive mRNA subtype intermixed at protein level
- New 'Innate' and 'Stromal' subtypes emerged



Ovarian Cancer: Deep proteomic analysis yields pathway activation correlated with overall survival

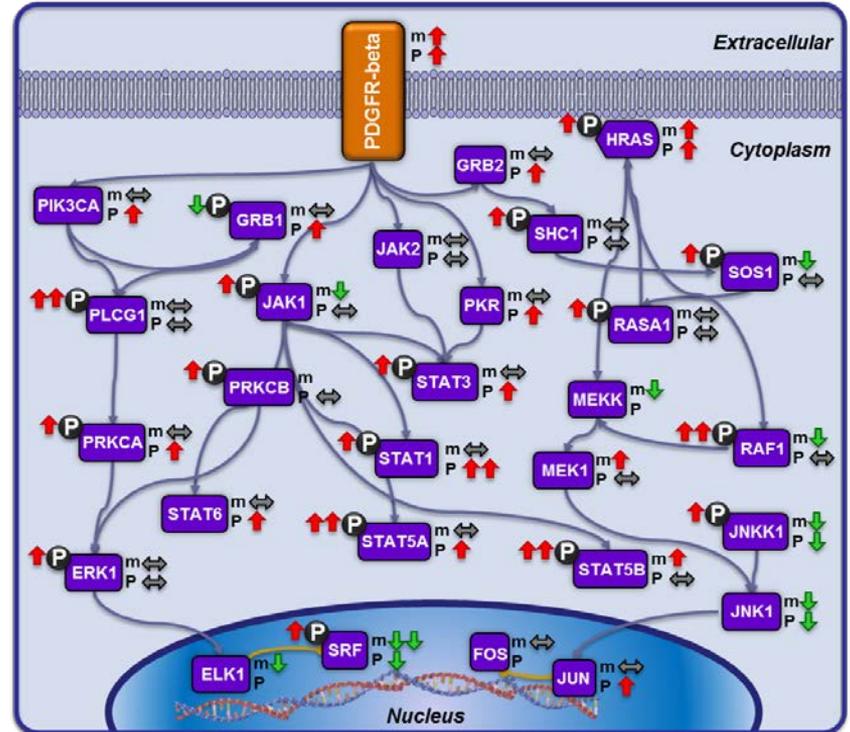


- NCI Pathway Interaction Database (214 signaling pathways)

- Significantly upregulated pathways with short OS
 - Protein data ($p < 0.05$)
 - Phosphorylation data ($p < 0.0001$)
 - mRNA data ($p < 0.05$)

- **Combining deep proteomic, phosphoproteomic and transcriptomic analysis better elucidated the proteogenomic complexity of pathway activation not obtainable at the subtype level.**

PDGFR pathway upregulation in TCGA **tumors** with short OS



m = mRNA	↑ = upregulated
P = protein abundance	↑↑ = significantly upregulated
Ⓟ = phosphoprotein	↓ = downregulated
	↓↓ = significantly downregulated
	↔ = no difference
	⊔ = not observed



Next steps (e.g.):

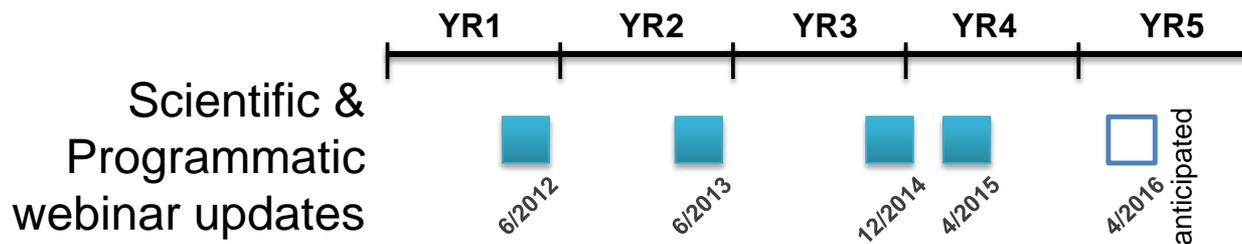
- **Q1. Can we rediscover the proteome subtypes?**
 - Deep analysis on independent collection (CPTAC prospective samples: 100 treatment-naïve tumors and normal)
- **Q2. Can we rediscover the short OS up-regulated pathways?**
 - Deep analysis on independent collection (CPTAC prospective)
- **Q3. Can targeted proteomic assay panels identify interesting proteome features?**
 - e.g. *Growth Factor Panel*: >30 proteins (non-modified and phospho) up-regulated in PDGFR & VEGFR associated with short OS (CPTAC prospective)

What have we learned

(observations from External Scientific Committee)

External Scientific Committee (ESC):

- Academia
- FDA
- NIH
- Industry

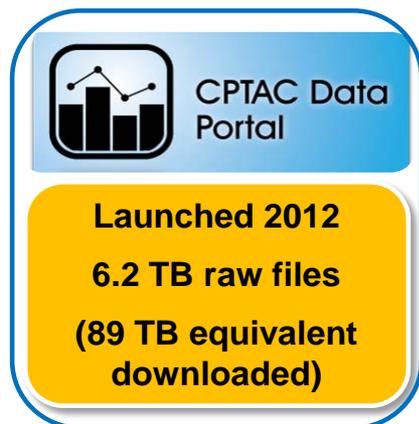


-
- CPTAC structure successful and innovative at addressing proteomics cancer research (*consortium of checks and balances*)
 - Accelerated adoption of standardized proteomic approaches by research community; critical step in marrying two crucial disciplines
 - Some PCCs better than others with innovative data analysis
 - Retrospective samples should be avoided, if possible

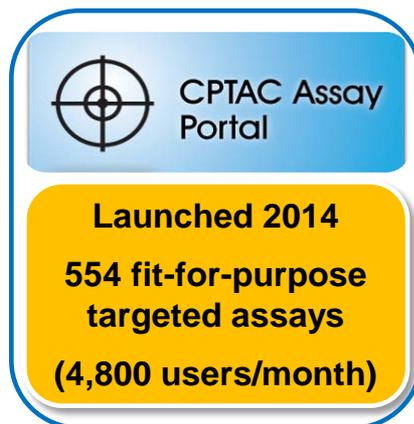
What have we learned

(observations from Independent Program Evaluation)

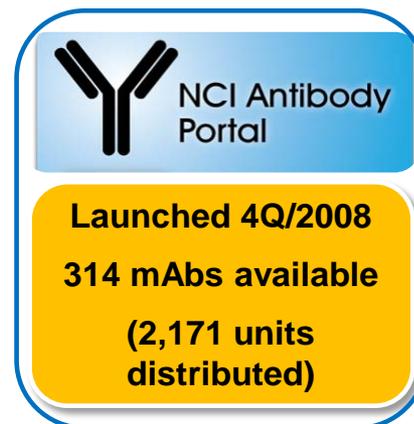
- Commissioned by the Office of Program Evaluation and Performance (NIH Office of the Director)
- Are CPTAC outputs (resources) utilized by scientific community?
 - Publication citations: too early to give a well-informed answer
 - partly due to data embargo dates:
CRC (pub Sept 2014); BRC (May 2015); OVC (Sept 2015)
 - **Other metrics...**



proteomics.cancer.gov



assays.cancer.gov



antibodies.cancer.gov



Part 2: What's next for CPTAC

- Process: Extensive input from External Scientific Committee members, Think Tank participants, and ongoing discussions with NCI Divisions, Centers and Offices program staff
- Consensus recommendations: Leverage investments in cancer genomics, by building on current achievements in cancer proteomics
 - (a) Supports an understanding of tumor proteogenomic complexity
 - (b) Addresses clinical/biological questions of drug response/toxicity prediction and resistance
 - (c) Accelerates proteomics science through community resources

Two Overarching Goals Addressing Specific Questions of Cancer

- **Goal 1: Improve our understanding of the proteogenomic complexity of tumors**

- Q. What's the association between genome and proteome?
- Q. How do signaling pathway components crosstalk (DNA, RNA, and protein/PTMs)?
- Q. What's the impact of genetic alterations on the proteome?

A. Proteome Characterization Centers (PCCs): extend CPTAC's approach to additional cancer types where questions remain on their proteogenomic complexity

- 5-6 cancer types; 100+ cases each (treatment-naïve CPTAC prospective collection); (*selection by extramural community - ESC members, CPTAC PIs, TCGA PIs, Think Tank participants*)

-
- Patient-Derived Models Repository program (*coordination with DCTD*)
 - Human Cancer Models Initiative (*coordination with CCG, DCTD, and DCB*)

Two Overarching Goals Addressing Specific Questions of Cancer

- **Goal 2: Improve our understanding of tumor resistance to therapy, and predicting treatment response**
(role of non-genetic factors)

- Q. Why do some individuals not respond or relapse to therapies, when genomics indicated otherwise?
- Q. What are the underlying mechanisms of resistance to therapies?

B. Proteogenomic Translational Research Centers (PTRCs):

CPTAC's approach to research models and clinical trial samples

- Applications to include well-conceived clinical/biological questions, access to clinical trial samples, and a proteogenomics research approach (*coordination with NCI's DCTD - CTEP and CDP*)

.....

C. Proteogenomic Data Analysis Centers (PGDACs)

- Work hand-in-hand with PCCs/PTRCs to develop innovative tools that process and integrate data across the entire proteome
Data*, assays and resources (goals 1 & 2) - community resources.
(**coordination with CCG and CBIIT*)

Structure and Budget

- Current total FY2015 budget is \$13M/yr (U24 PCCs)



- Proposed path forward and recommended budget is \$13M/yr
 - Reduce and optimize **PCCs** by focusing on data generation. Budget is \$4.0M/yr (U24)
 - Proteogenomic translation to be performed by **PTRCs**. Budget is \$4.5M/yr (U01)
 - Data integration/analysis to be performed by specialized **PGDACs**. Budget is \$4.5M/yr (U01)

Key Contributors

DCTD, Cancer Diagnosis Program

- Barbara Conley
- James Tricoli
- Tracy Lively
- Tawyna McKee
- Brian Sorg
- Irina Lubensky
- Magdalena Thurin
- Kim Jessup
- Helen Moore

DCTD, Biometric Research Branch

- Lisa McShane

DCTD, Cancer Therapy Evaluation Program

- Jeff Abrams
- Shakun Malik
- James Zwiebel
- Margaret Mooney
- Percy Ivy
- Jeffrey Moscow
- Ming Song
- Jo Anne Zujewski
- Elise Kohn

OD, Center for Cancer Genomics

- Lou Staudt
- Jean C. ZenKlusen

DCTD, Translational Research Program

- Toby Hecht
- Peter Ujhazy
- Andrew Hruszkewycz
- Tamara Walton
- Igor Kuzmin
- Steve Nothwehr
- Julia Arnold
- Leah Hubbard
- Rajeev Agarwal



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The Genomic Data Analysis Network (GDAN)

Lou Staudt

June 24, 2015

A vertical strip on the left side of the slide shows a close-up, slightly blurred view of a stethoscope's chest piece and tubing, set against a dark background.

Computational Genomics – A Growing Necessity in Cancer Research

- TCGA production:
 - 33 tumor types and 11,500 cases
 - 2.5 petabytes (PB) of data
- Successful analysis and utilization of TCGA data required:
 - Experiments performed utilizing strict standardized protocols
 - Data in structured formats and available in public databases
 - Formation of Analysis Working Groups, with expertise in computational genomics, tumor biology and clinical oncology
- Genome Data Analysis Centers (GDACs) have been indispensable for progress in TCGA



Genome Data Analysis Centers (GDACs)

Generation of bioinformatics tools
for the research community

Firehose: An Automated Pipeline

Analysis Overview for Breast Invasive Carcinoma

Maintained by [TCGA GDAC Team](#) (Broad Institute/Dana-Farber Cancer Institute/Harvard Medical School)

Overview

- Introduction
- Summary

Note: These results are offered to the community as an additional reference point, enabling a wide range of cancer biologists, clinical investigators, and genome and computational scientists to easily incorporate TCGA into the backdrop of ongoing research. While every effort is made to ensure that Firehose input data and algorithms are of the highest possible quality, these analyses have not been reviewed by domain experts.

Results

Sequence and Copy Number Analysis

Copy number analysis (GISTIC2)

View Report | There were 847 tumor samples used in this analysis: 26 significant arm-level results, 28 significant focal amplifications, and 38 significant focal deletions were found.

Mutation Analysis (MutSig)

View Report | MAF used for this analysis: [BRCA_focal_analysis_wt.c...](#)

Clustering Analysis

Clustering of copy number data: consensus NMF

View Report | The most robust consensus NMF clustering of 847 samples using the 66 copy number focal regions was identified for $k = 5$ clusters. We computed the clustering for $k = 2$ to $k = 8$ and used the cophenetic correlation coefficient to determine the best solution.

Clustering of Methylation: consensus NMF

View Report | The 8506 most variable methylated genes were selected based on variation. The variation cutoff was set for each tumor type empirically by fitting a bimodal distribution. For genes with multiple methylation probes, we chose the most variable one to represent the gene. Consensus NMF clustering of 847 samples and 8506 genes identified 6 subtypes with the stability of the clustering increasing for $k = 2$ to $k = 5$ and the average silhouette width calculation for selecting the robust clusters.

Clustering of RPPA data: consensus NMF

View Report | The most robust consensus NMF clustering of 408 samples using the 150 most variable proteins was identified for $k = 3$ clusters. We computed the clustering for $k = 2$ to $k = 8$ and used the cophenetic correlation coefficient to determine the best solution.

Clustering of RPPA data: consensus hierarchical

View Report | The 150 most variable proteins were selected. Consensus average linkage hierarchical clustering of 408 samples and 150 proteins identified 7 subtypes with the stability of the clustering increasing for $k = 2$ to $k = 8$.

[Tracking System](#)



Labels: None

13 Child Pages

- Contact Us
- DCC Interactions
- Nozzle
- Pipeline Docs
- Presentations

<http://gdac.broadinstitute.org>

[w/change](#) [show comment](#)

... of the [Broad Institute's](#) Genome Data Analysis Center (GDAC). On behalf of [The Cancer Genome Atlas \(TCGA\)](#), we've designed and [analysis pipelines](#) which pump terabyte-scale genomic datasets through scores of quantitative algorithms, in the hope of accelerating the See the [dashboards](#) below for details of the latest monthly runs, or [this presentation](#) for more background information. Note that this site constitutes agreement to [this data usage policy](#).

2012_08_25 stddata Run

2012_08_25 analyses Run

Notes	# Datasets	% Processed	Download	AnalysisReport	# Pipelines	% Successful	Download
LOX	20	100%	Download	26,42	25	100%	Download
BSA							
ESC							
BREAD							
LC							
BM							
LCC							
BC							
PL							
DL							
LG							
LHC							
LUAD							
LUSC							
OV							
PMAD							
PRAD							
SARC							
SKCM							
STAD							
THCA							
UCEC							
BANCANCER							

Breast Invasive Carcinoma: Copy number analysis (GISTIC2)

Maintained by [Dan DiCara](#) (Broad Institute)

Overview

Introduction

Summary

There were 847 tumor samples used in this analysis: 26 significant arm-level results, 28 significant focal amplifications, and 38 significant focal deletions were found.

Results

Focal results

Figure 1. Genomic positions of amplified regions: the X-axis represents the normalized amplification signals (top) and significance by Q value (bottom). The green line represents the significance cutoff at Q value = 0.25.

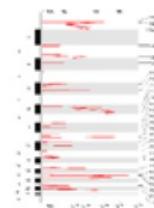


Table 1. Amplifications Table - 28 significant amplifications found. Click the link in the last column to view a comprehensive list of candidate genes. If no genes were identified within the peak, the nearest gene appears in brackets.

Cytoband	Q value	Residual Q value	Wide Peak Boundaries	# Genes in Wide Peak
18q11.23	2.3876e-166	5.3087e-152	chr11:26400218-69487994	2
8q24.21	1.6156e-78	1.6156e-78	chr8:128657453-128779930	1
17q11.2	7.9055e-120	1.216e-69	chr17:37789433-3789907	9
8p11.23	3.4851e-77	3.5102e-68	chr8:37487106-37604543	3

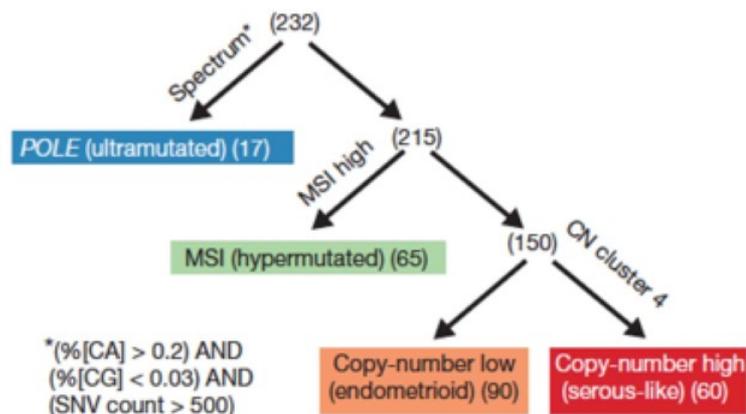
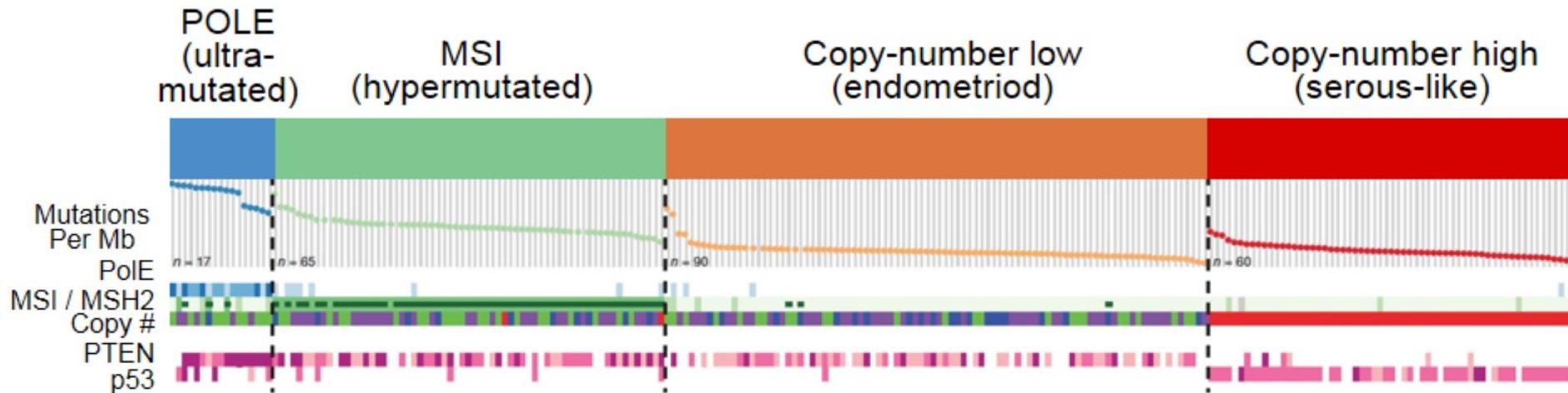


Genome Data Analysis Centers (GDACs)

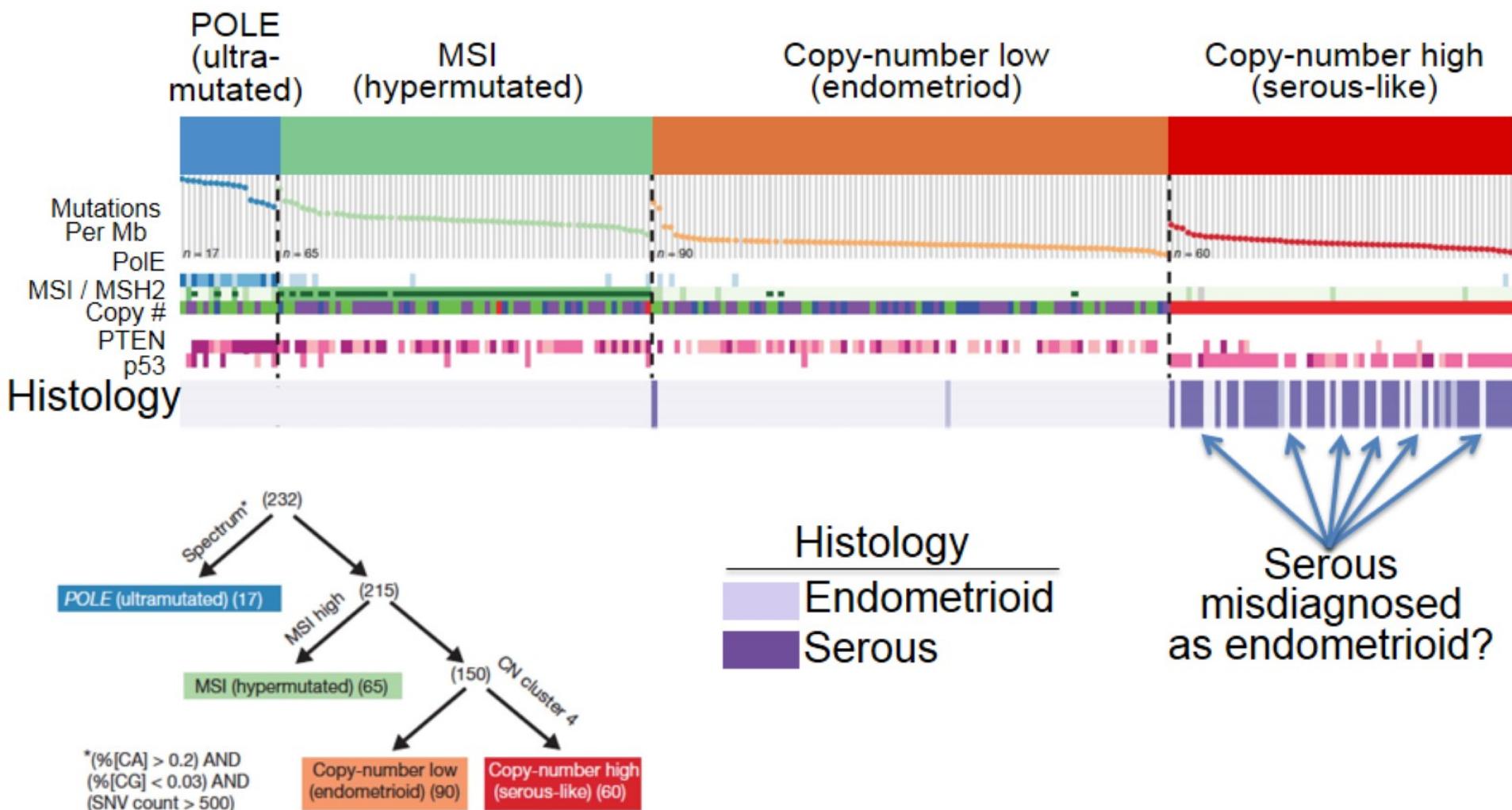
Data analysis for Analysis Working Groups

Generation of clinically meaningful
molecular subgroups of cancer

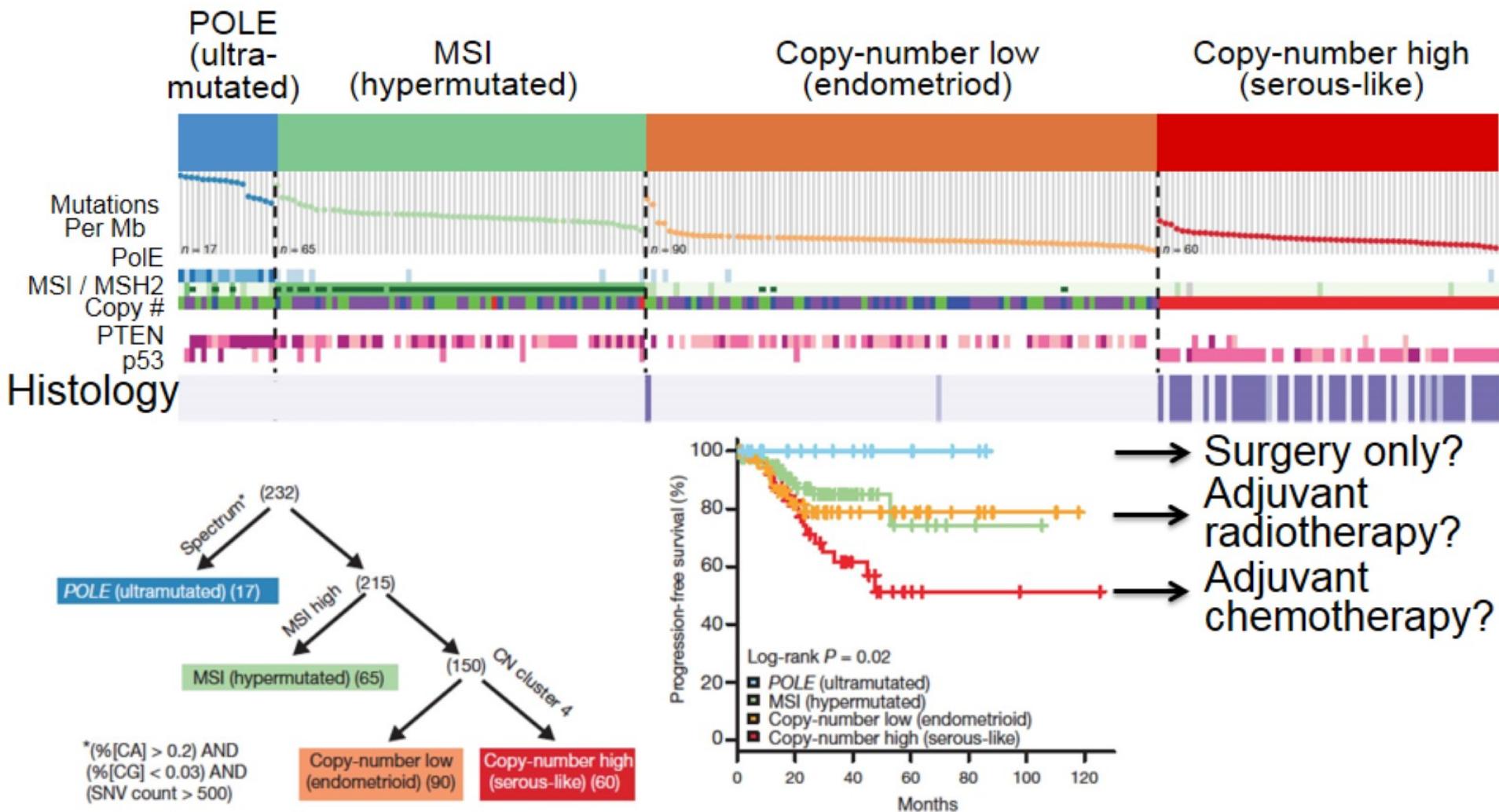
Four Molecular Subgroups of Endometrial Cancer Defined by Integrative Analysis



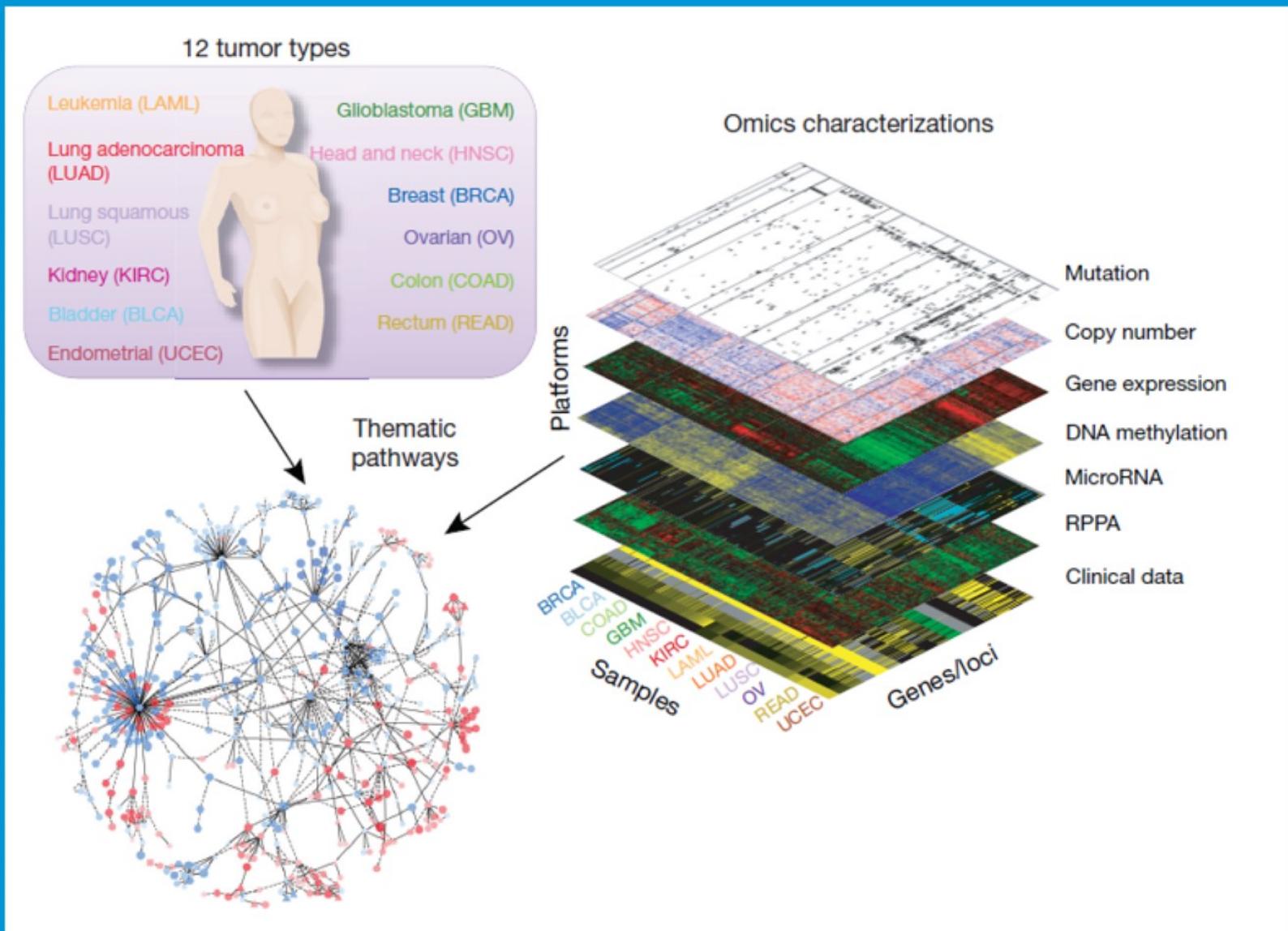
Molecular Subgroups Refine Histological Diagnosis Of Endometrial Carcinoma



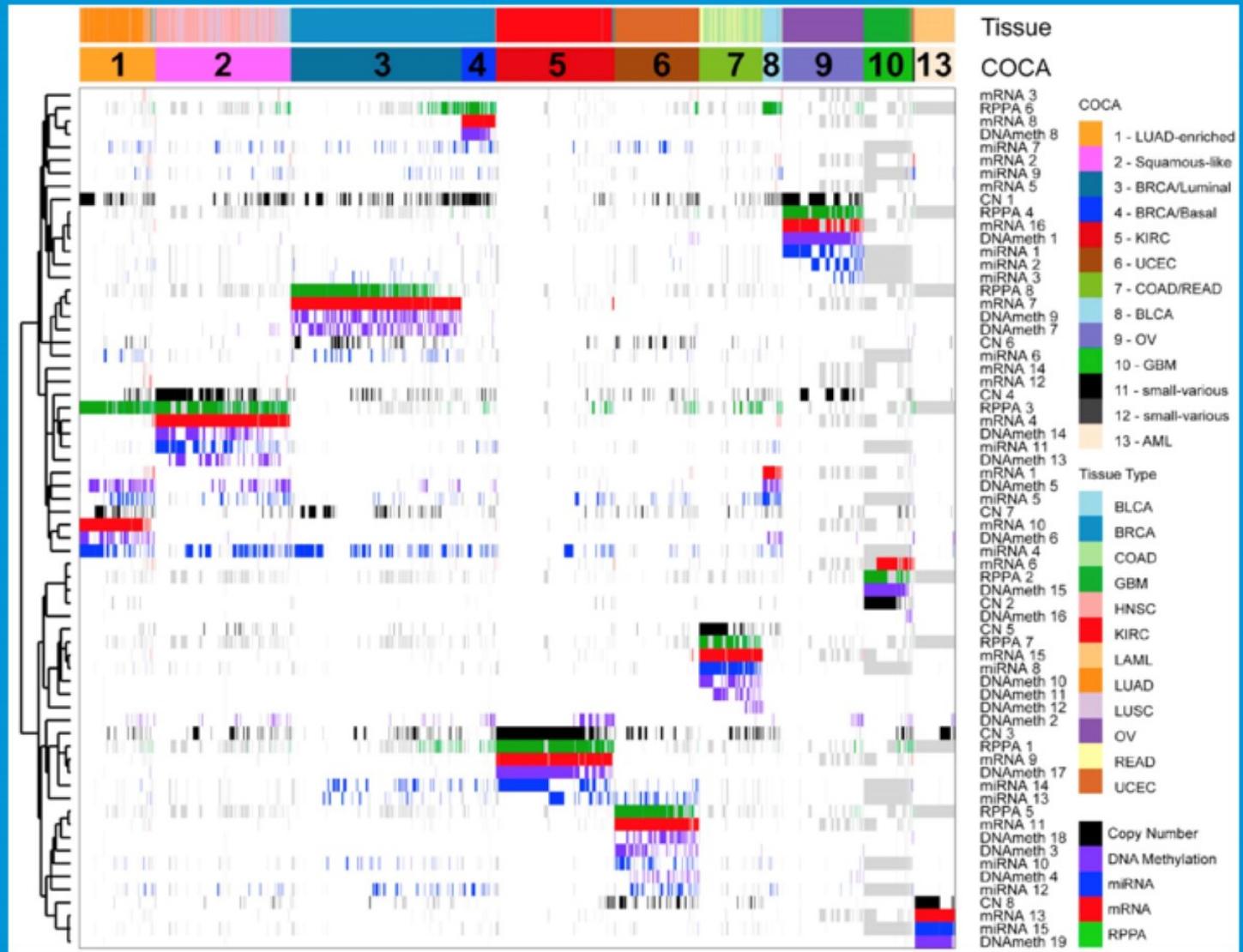
Molecular Diagnosis of Endometrial Cancer May Influence Choice of Therapy



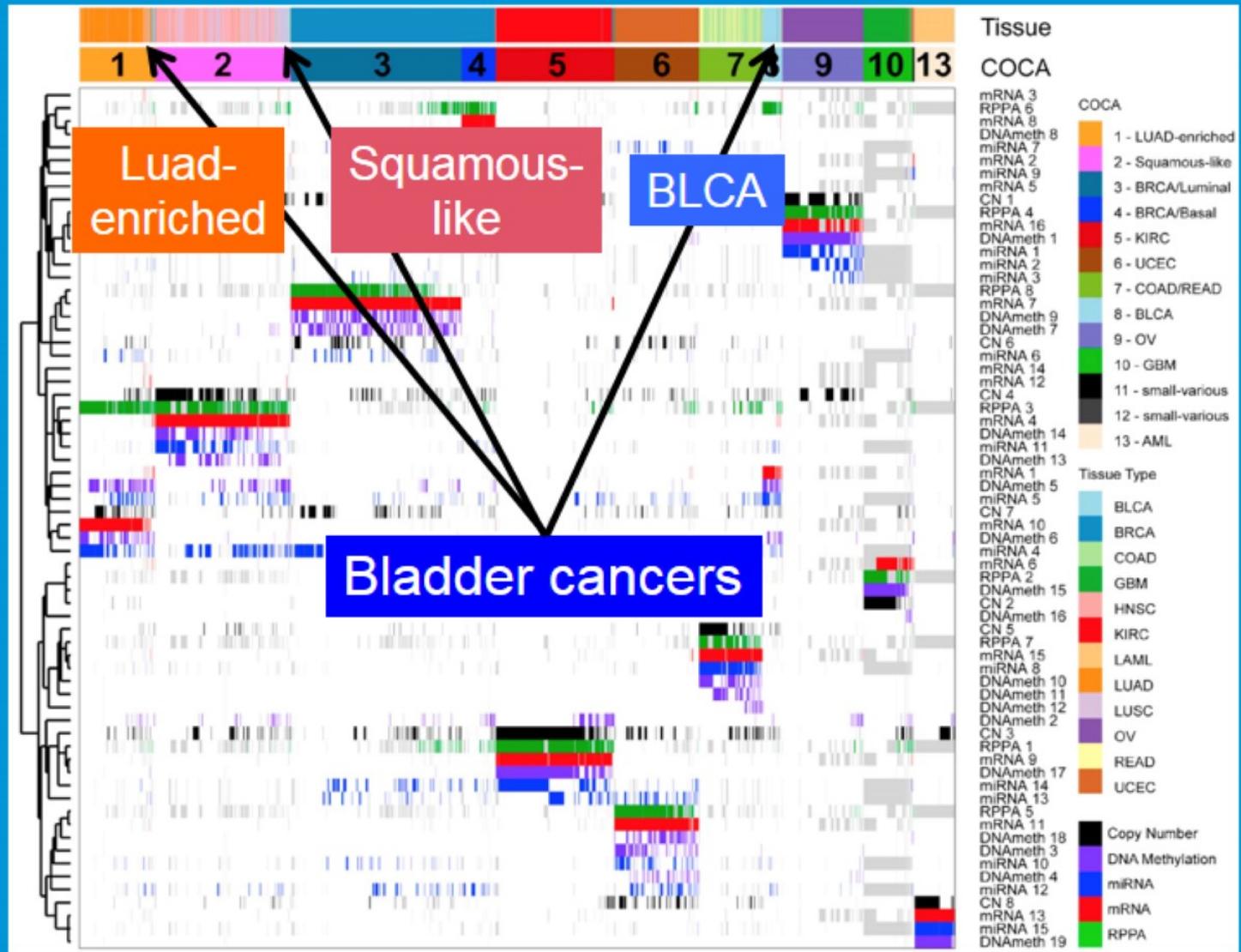
Integration Matters



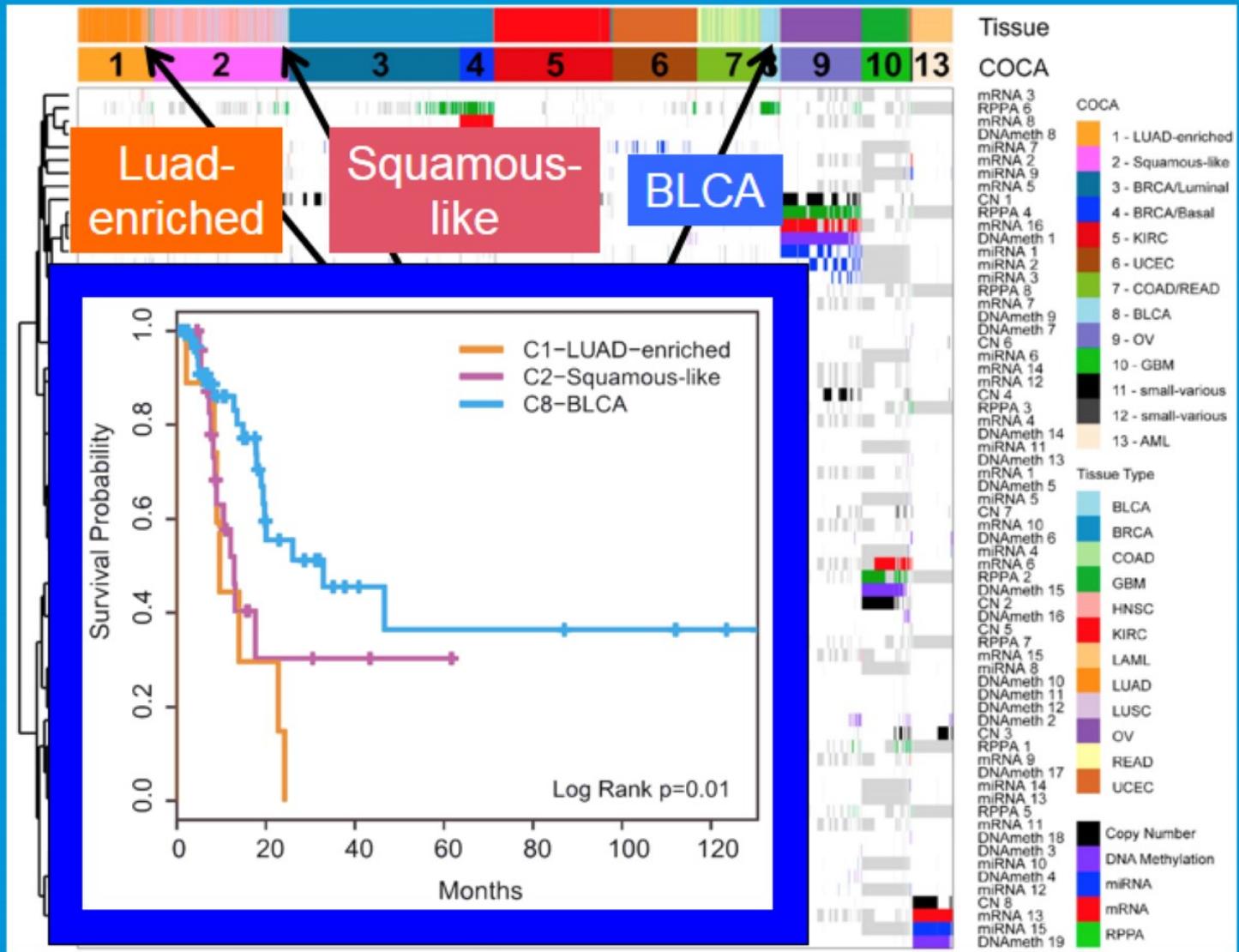
PanCan Analysis Reveals Clinically Distinct Bladder Cancer Subtypes



PanCan Analysis Reveals Clinically Distinct Bladder Cancer Subtypes



PanCan Analysis Reveals Clinically Distinct Bladder Cancer Subtypes



A vertical strip on the left side of the slide shows a close-up, slightly blurred view of a stethoscope's chest piece and tubing, set against a dark background.

Computational Genomics for Center for Cancer Genomics Initiatives

- CCG initiatives will:
 - Conduct comprehensive genome-wide analyses of molecular alterations in cancers
 - Utilize multiple platforms to profile the genome, transcriptome and epigenome of cancer
- CCG goals include:
 - Identify genomic alterations that influence the development of cancer and the response to treatment
 - Collaborate with other NCI Divisions and Centers to conduct the most meaningful genomic studies
 - Support the Precision Medicine Initiative

The CCG Genomics Pipeline

Cancer Biopsies

Biospecimen Core Repository (BCR)

Tumor Pathology QC

- % Tumor Nuclei
- % Necrosis
- Dx Confirmation via histology and pathology report

Molecular Analyte QC

- Spectrophotometry
- RNA Bioanalyzer
- Electrophoresis
- Genotyping

Genome Characterization Centers

Exome seq

Whole genome seq

RNA-seq

DNA Methylation

Genome Data Analysis Network (GDAN)

Genetic aberrations

Mutations
Copy number
Translocations

Data analysis:

Molecular subgroups
Co-occurrence / exclusion
Comparison to TCGA

Data integration:

Functional vs. structural
Master regulator analysis
Pathway analysis

Projects Involving the GDAN

- CCG initiatives (some with other NCI Divisions):
 - Cancer Driver Discovery Program (CDDP)
 - The Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trials (ALCHEMIST)
 - Exceptional Responders (in collaboration with DCTD)
 - Clinical Trials Sequencing Program (in collaboration with DCTD)
 - Environment and Genetics in Lung Cancer Etiology (EAGLE, in collaboration with DCEG)
- The GDAN can be used to support any NCI project that utilizes the CCG genomics pipeline

Composition of the GDAN

- Processing GDAC
 - Develops and implements appropriate bioinformatic systems for rapid high-throughput processing
 - Operates closely with the NCI Genomic Data Commons (GDC) to generate primary genomic results
 - One center will be awarded
- Visualization GDACs
 - Provides user-friendly bioinformatics tools and data portals for the exploration of results
 - Explores new methods to integrate data
 - Two centers will be awarded
- Specialized GDACs
 - Provides in-depth expertise on individual platforms
 - Provides analytical support to Analysis Working groups
 - Eleven centers will be awarded

Mechanisms of Award & Budget

- All awards will be U24 Cooperative Agreements
- Budget is as follows (in thousand dollars):

GDAC Type	Award Number	Amount /Year	FY2016	FY2017	FY2018	FY2019	FY2020
Process	1	1,000	1,000	1,000	1,000	1,000	1,000
Visual	2	1,000	2,000	2,000	2,000	2,000	2,000
Special	11	500	5,500	5,500	5,500	5,500	5,500
		Total	8,500	8,500	8,500	8,500	8,500
Grand Total		42,500					

Justification for the GDAN RFA

- TCGA experience suggests that data analysis in large-scale genomic characterization programs requires a coordinated group of experts in computational genomics
- This coordinated network requires a detailed statement of needs, including time lines and deliverables
- It is unlikely that such a network would evolve from a disparate collection of investigator-initiated grants
- The GDAN will support and stimulate the development of computational genomics tools and methodologies for the research community

Justification for Cooperative Agreement

- The CCG genomics pipeline requires coordination of:
 - Biospecimen processing
 - Genomic characterization of analytes
 - Analysis of the resulting data
- This coordination is maintained by the CCG Program staff working with the Analysis Working Groups.
- A cooperative agreement will allow CCG Program staff to deploy GDAN centers strategically to meet NCI needs
- A cooperative agreement will ensure that all results will be made publically available on a defined timeline
- The cooperative agreement will require that all bioinformatics tools be open-source and publically available

Evaluation Criteria

- The impact of the GDAN will be judged by:
 - Successful and timely support of the Analysis Working Groups (AWGs) for each CCG/NCI project
 - Cancer relevance of publications supported by the GDAN, as measured by citations and other metrics
 - Adoption of the bioinformatics tools generated by the GDAN for data processing and visualization
 - Training and support of trainees in computational

A vertical strip on the left side of the slide shows a microscopic view of a cell or tissue structure, possibly a cross-section of a vessel or a similar biological structure, with a central dark spot and surrounding lighter, textured areas.

Questions?

NCI Center for Global Health Update on U.S. – China Partnership in Cancer Research

**Board of Scientific Advisors &
National Cancer Advisory Board**

**Ted Trimble, MD, MPH
NCI Center for Global Health
June 24, 2015**

Mao Zedong & Richard Nixon, 1971



Deng Xiaoping & Jimmy Carter, 1979



Brief History

- **1979** **US-China Agreement on Cooperation in Science and Technology**
 - **1980** **Atlas of Cancer Mortality in the People's Republic of China**
 - 1981- Launch of epidemiologic studies of lung, esophagus, stomach, liver cancers, and studies of environmental and occupational exposures
 - 1985 Linxian Nutrition Intervention Trial (NIT) launched
 - 1986 Shanghai Health Study Cohort launched
 - 1993 NIT results published
 - 1997 Study of hematologic cancers in benzene exposed worker published
- 
- **2008** **NCI Office of China Cancer Programs, Beijing, Dr. Julie Schneider**
 - 2010 MOU NCI–Beijing Tiantan Hosp (Chinese Cancer Genome Consortium)
 - 2010 MOU NIH–National Science Foundation of China (NSFC)
 - 2011 MOU HHS–Ministry of Science and Technology (MOST)
 - **2011** **NCI Center for Global Health, Beijing, East Asia, Dr. Ann Chao**
 - 2012 MOU NCI–Chinese National Cancer Center
 - **2015** Ongoing research and training cooperation

Cancer Incidence, China, 2011

Rank	Male			Female		
	Site	Cases	ASR*	Site	Cases	ASR*
1	Lung	441,364	48.44	Breast	248,620	28.51
2	Stomach	296,419	32.62	Lung	209,689	21.93
3	Liver	264,635	29.30	Colorectum	131,840	14.02
4	Esophagus	205,560	22.47	Stomach	124,070	13.21
5	Colorectum	178,404	19.70	Liver	90,960	9.64
6	Bladder	53,074	5.82	Cervix	87,982	10.40
7	Prostate	49,007	5.33	Esophagus	85,678	8.85
8	Pancreas	45,385	4.99	Thyroid	67,788	8.70
9	Brain, CNS	43,289	5.22	Uterus	57,709	6.46
10	Lymphoma	41,298	4.80	Ovary	45,233	5.35

Data Source: 2013 Chinese Cancer Registry Annual Report

* ASR – age standardized rate, Segi standard population

Cancer Mortality, China, 2011

Rank	Male			Female		
	Site	Cases	ASR*	Site	Cases	ASR*
1	Lung	364,432	39.94	Lung	164,721	16.68
2	Liver	239,218	26.38	Stomach	90,792	9.21
3	Stomach	206,704	22.69	Liver	83,199	8.61
4	Esophagus	154,587	16.86	Esophagus	64,371	6.38
5	Colorectum	86,427	9.40	Colorectum	63,295	6.26
6	Pancreas	40,580	4.43	Breast	60,473	6.57
7	Brain,CNS	28,542	3.35	Pancreas	32,143	3.21
8	Leukaemia	27,907	3.46	Cervix	23,375	2.59
9	Lymphoma	25,066	2.84	Brain,CNS	22,234	2.54
10	Bladder	20,949	2.23	Leukaemia	19,708	2.45

Data Source: 2013 Chinese Cancer Registry Annual Report

* ASR – age standardized rate, Segi standard population

Research – Addressing Major Cancer Burdens

Lung Cancer

- Occupational Cohort of Tin miners in Yunnan Province
- Genetic susceptibility and environmental exposures in women who never smoked tobacco

Upper Gastrointestinal Cancers

- Studies of etiology, early detection, and treatment
- Nutritional Intervention Trial

Liver Cancer

- Epidemiology
- Genetic basis of hepatocellular carcinoma, diagnostic markers, potential treatment targets

Research – Addressing Major Cancer Burdens

Colorectal Cancer

- Microbiome and adenoma, colorectal cancer screening

Breast Cancer

- Breast density and tumor molecular subtypes

Nasopharyngeal Cancer in Southern China

- Familial, viral, dietary, and environmental risk factors

Hematologic Cancers

- Lymphoma subtypes in relation to occupational and environmental exposures
- Benzene-exposed workers; study results were instrumental in modifying US EPA rulings

Research Co-Funding

NIH – National Science Foundation of China (NSFC) US-China Program for Biomedical Research Cooperation

Objective

- Build US-China scientific cooperation and teams to address a common question
- Assess the benefits and challenges of co-managing a collaborative program

Year 1 (FY2011)

- Extramural 1-year administrative supplements, intramural 1-year new awards
- NIH ~\$3 million (NCI, NIAID, OAR), NSFC ~9 million RMB

Year 2 (FY2012)

- Extramural 1-year administrative supplements, intramural 1-year new awards
- NIH ~\$4 million (NCI, NIAID, OAR, NIMH), NSFC ~12 million RMB

Year 3 (FY2013)

- Extramural 3-year R01 awards
- NIH ~\$5 million (NCI, NIAID, OAR, NIMH, NINDS), NSFC ~15 million RMB

Evaluation

Research Co-Funding

NIH – Chinese Ministry of Science and Technology (MOST)

Objective

- Build new US-China cooperation in biomedical research funding, including clinical research
- Exchanges information on research funding governance, infrastructure, and management

Status

- MOST engagement with NIAID
- 2014 MOST leadership visit to NIH in 2014 with leaders of 4 National Clinical Research Centers , issued call for proposals from National Clinical Research Centers working with NIH

Training and Capacity Building

In the US

- Chinese post-doctoral fellows at NCI, NCI-designated Cancer Centers, and universities
- Chinese researchers and visiting fellows at NCI, NCI Cancer Centers, and universities
- Participation in NCI's Summer Principles and Practices of Cancer Prevention and Control Course

In China

- Training through working on joint research
- Joint workshops (select examples)
 - Media workshop for journalists
 - Using cancer registry data to inform research and cancer prevention and control policy
- Training of US Fogarty and Fulbright fellows

Role of NCI Center for Global Health

Advocate for research and implementation of research results

- HPV vaccine approval and implementation in China, tobacco control, etc.
- Building and sustaining national clinical research networks
- Partnerships in China and internationally (WHO, IARC, etc.)

Convene

- Partners within and across disciplines, institutions, countries, regions

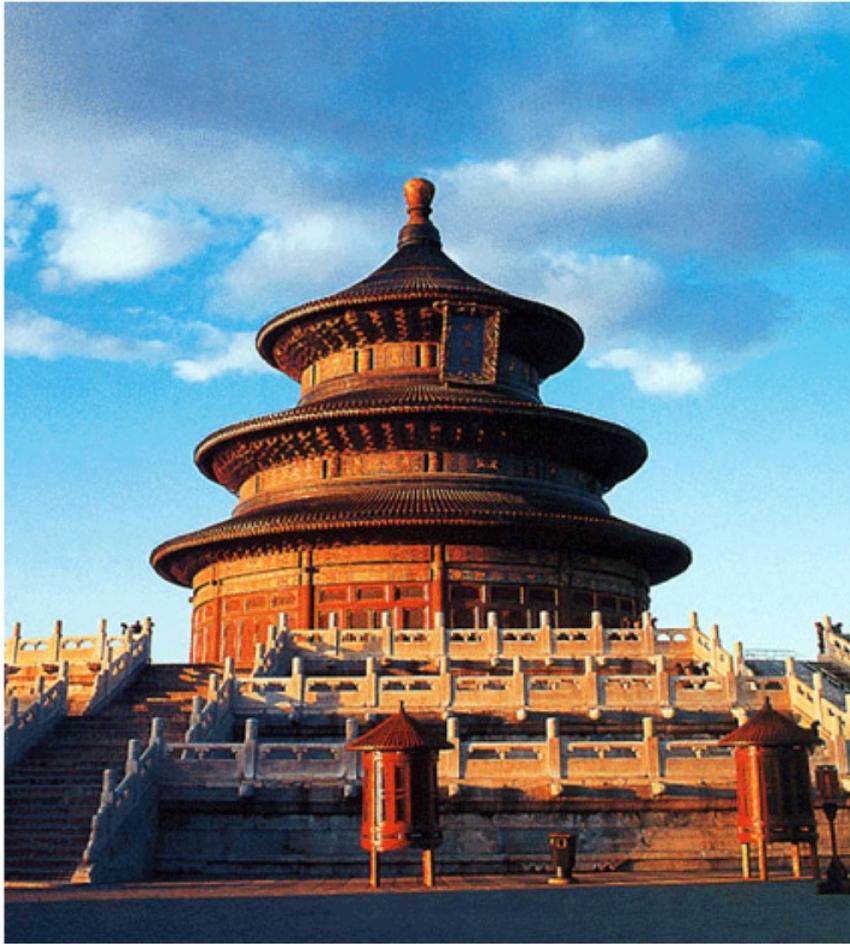
Facilitate

- Ongoing research collaborations and help address needs of intramural and extramural scientists in the US, China, and elsewhere
- Opportunities for scientific exchange
- New initiatives in cancer research, prevention and control

Explore

- Outstanding scientists and opportunities for research, funding, advocacy
- Training and capacity building
- Cooperation in China's global health work

China-US partnership in cancer research





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Center for Cancer Research: Chinese Interactions

Lee J. Helman, Scientific Director for Clinical Research

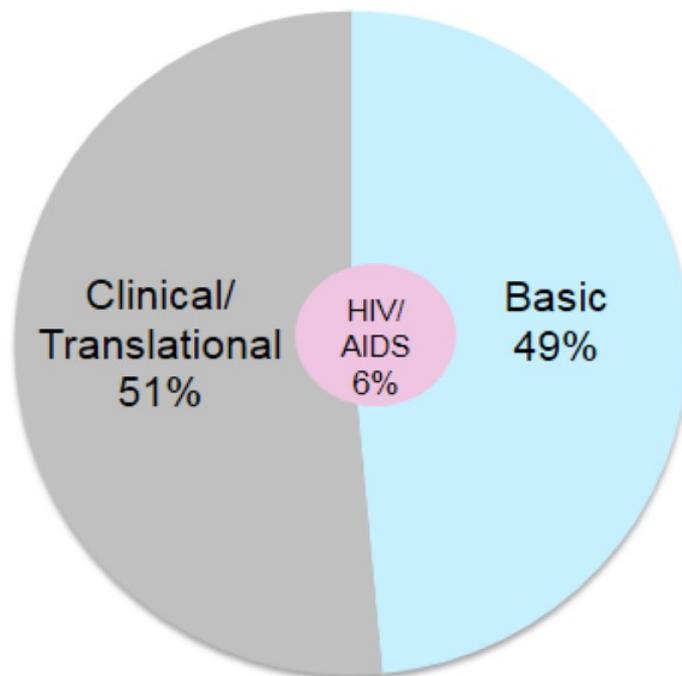
Xin Wei Wang, Laboratory of Human Carcinogenesis

June 2015



CCR Vision

Integrate basic, translational, and clinical research to make cancer preventable, curable, or chronically manageable.





Distinctiveness of NCI's CCR Derives from a Convergence of Multiple Attributes

- **Sustained support for high-risk, high-impact research**
- **Highly interactive, interdisciplinary culture for basic and clinical scientists:**
 - generation of new knowledge
 - efficient bench to bedside to bench translation
 - development of new technologies
- **Access to the world's largest cancer-focused clinical research center**
- **Focus on rare cancers and underserved patient populations**
- **Borderless collaborations that enable joint ventures among cancer research's thought leaders within and outside the NCI**
- **Flexibility to rapidly reallocate resources**
- **Multi-faceted training for the next generation of scientific leaders**



CCR:China Connections

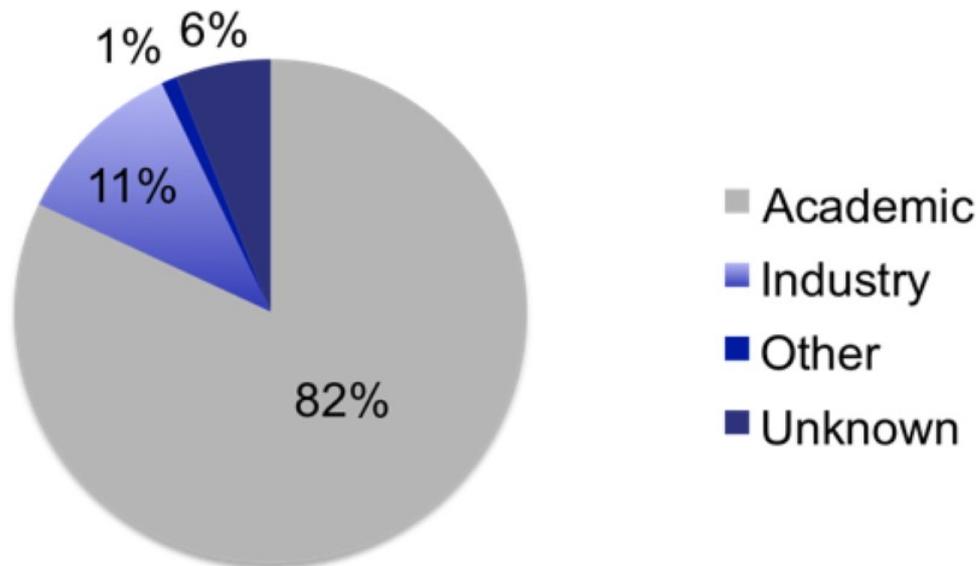
- **Personnel**
- **Collaborations**
- **Via HHS/NIH/NCI**



CCR:China Connections

- Personnel**

- 10% of CCR PIs are of Chinese descent
- Over 150 recent alumni (over the last 5 years) are now working in China





CCR:China Connections

Collaborations

• In 2014, 18 different PIs had active collaborations with 33 Chinese investigators at 28 different institutions

NASOPHARYNGEAL CARCINOMA CHEMOATTRACTANT RECEPTORS
LIVER CANCER
 KIR/HLA ABC TRANSPORTERS
BLADDER CANCER
 PROTEOGLYCAN RECEPTOR
NEUROBLASTOMA
 SCREENING NATURAL COMPOUNDS
ALS BRAIN CANCER
 SMURF PROTEINS
HPV HBV HIV
 TNF-INDUCED NECROSIS WP1 GENE

- 2nd China Medical School
- Beijing Genome Institute
- Beijing University First Hospital
- Beijing University of Technology
- Chang Gung University
- China Academy of Traditional Chinese Medicine
- China Agriculture University
- Chinese Academy of Medical Sciences
- East China Normal University
- Fudan University
- Guanganmen Hospital
- Hong University of Science and Technology
- Institute for Nutritional Sciences
- Institute of Biomedicine and Biotechnology
- Institute of Pathology
- Institute of Virology
- Liver Cancer Institute
- Nanjing Medical University
- National Center of Biomedical Analysis
- Natl. Cancer Centre Duke-NUS
- Ocean University
- Shanghai Institute of Biochemistry and Cell Biology
- Shengjing Hospital of China Medical University
- Shenyang Pharmaceutical University
- State Key University
- Sun Yat-Sen University
- University of Hong Kong
- Zhejiang University



CCR:China Connections

- **Via HHS/NIH/NCI**
 - Participated in or organized symposia in China
 - Co-funded project announcements
 - NIH/Ministry of Science and Technology (MOST)
 - NIH IRP
 - US-China Program for Biomedical Research Cooperation a.k.a “Intramural to China”



Xin Wei Wang, Ph.D.
Deputy Chief
Laboratory of Human
Carcinogenesis

**Collaborative Studies
Between NCI and Fudan
University**

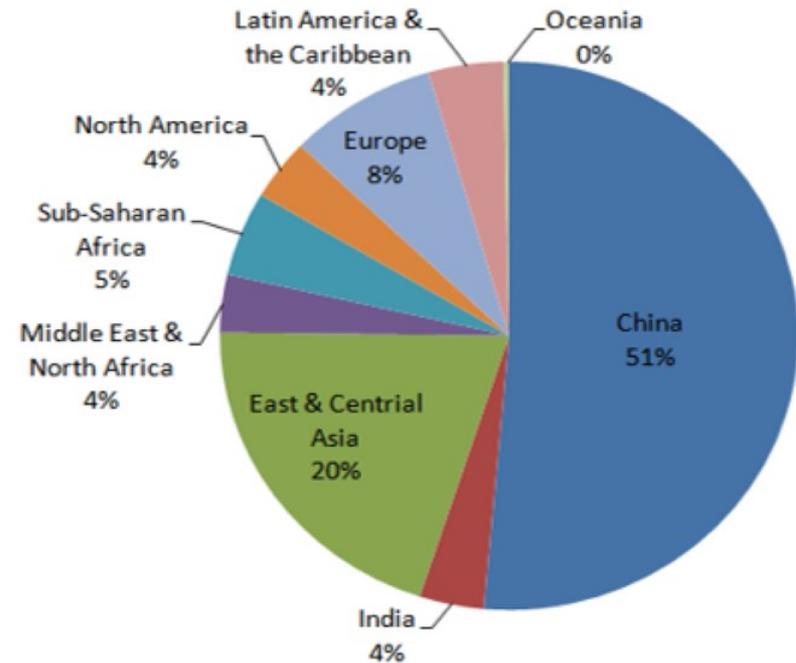
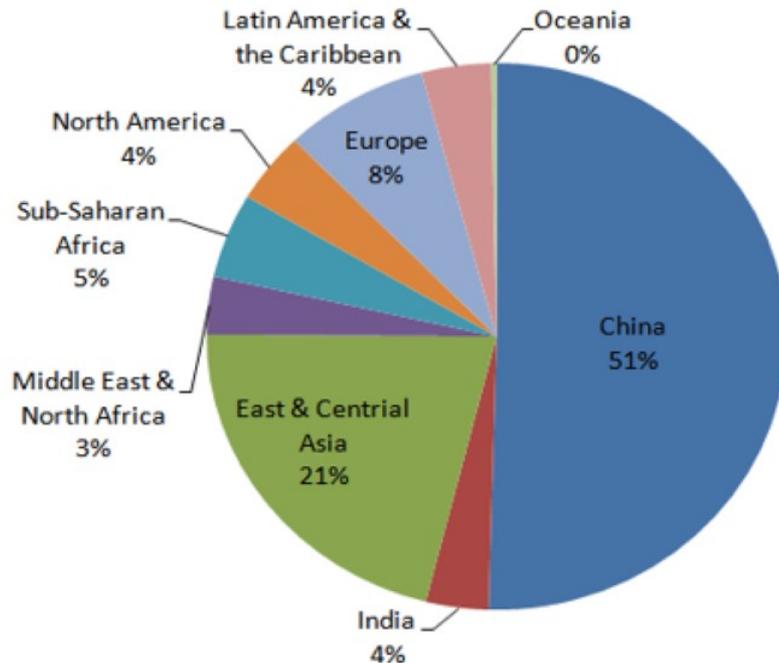
Liver Cancer is the Second Leading Cause of Cancer-related Death Worldwide



Steward BW & Wild CP, World Cancer Report 2014
www.who.int

Incidence: 782,000 new cases

Mortality: 746,000 deaths

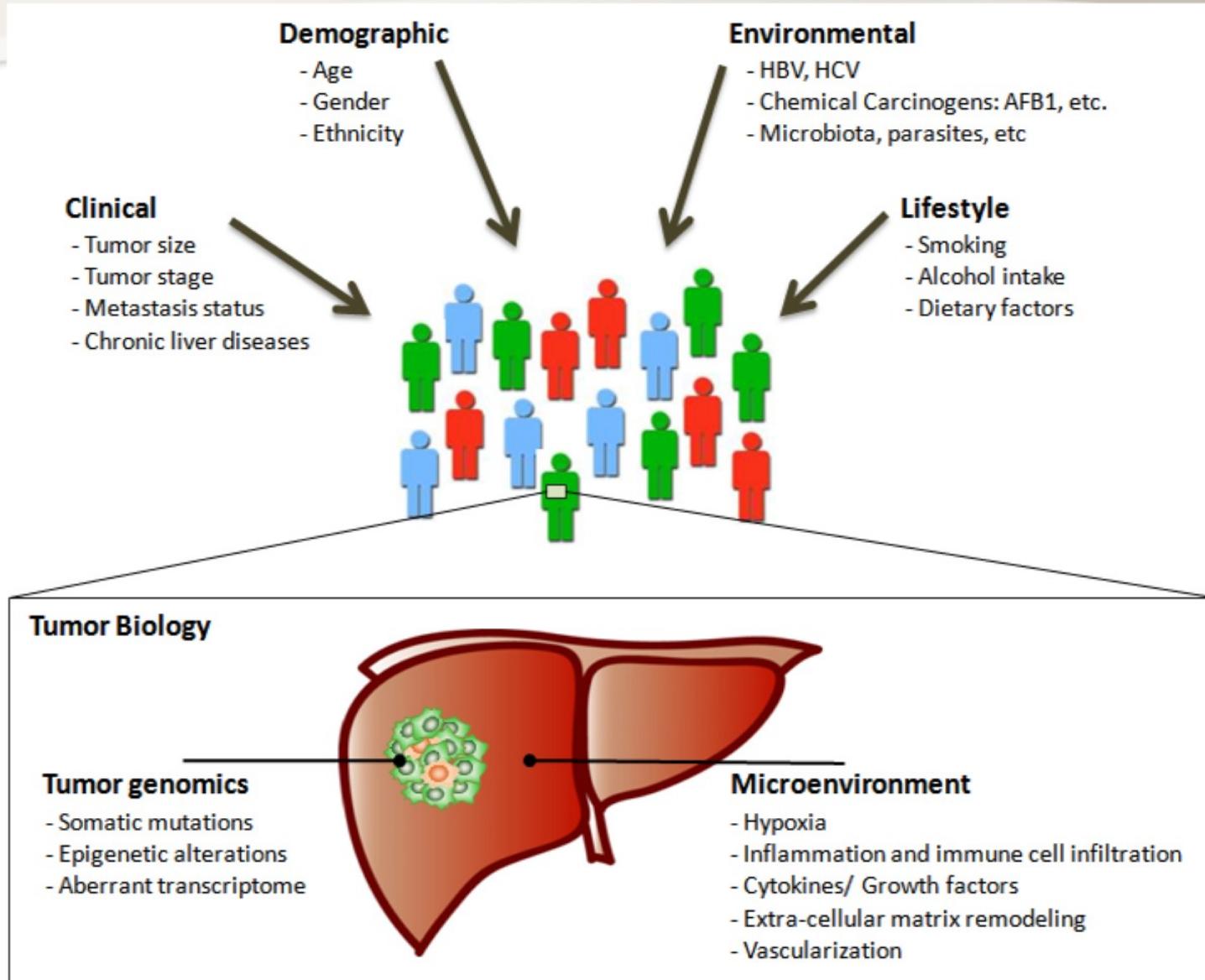


A liver cancer patient dies every 42 seconds

The Etiology and Features of Liver Cancer Heterogeneity



Sonya Parpart



Collaborative Studies Between NCI and Fudan University (1999-present)



- 1999: Established a formal collaboration between the Liver Carcinogenesis Research Group of the National Cancer Institute and the Liver Cancer Institute (LCI) of Fudan University (Dr. Zhao-You Tang)
- 2009: Jointly established a Personalized Liver Cancer Care and Research Center (PLCCRC) to perform genomic and genetic screens of liver cancer patients to identify new diagnostic biomarkers for molecular re-staging and treatment stratification
- 2009: Launched a multi-center RCT to assess the use of biomarker-guided adjuvant therapy in HCC patients
- Multiple collaborations with other LCI investigators including 3 formal Collaboration Agreements: Dr. Lun-Xiu Qin (Prof. of Surgery), Dr. Jia Fan (Director of Zhongshan Hospital), Dr. Qin-Hai Ye (Prof. of Surgery), Dr. Hui-Chuan Sun (Prof. of Surgery), Dr. Jian Zhou (Prof. of Surgery)
- Hosted and mentored 6 Visiting Fellows; including 5 MD/PhD students



Timeline and Milestones

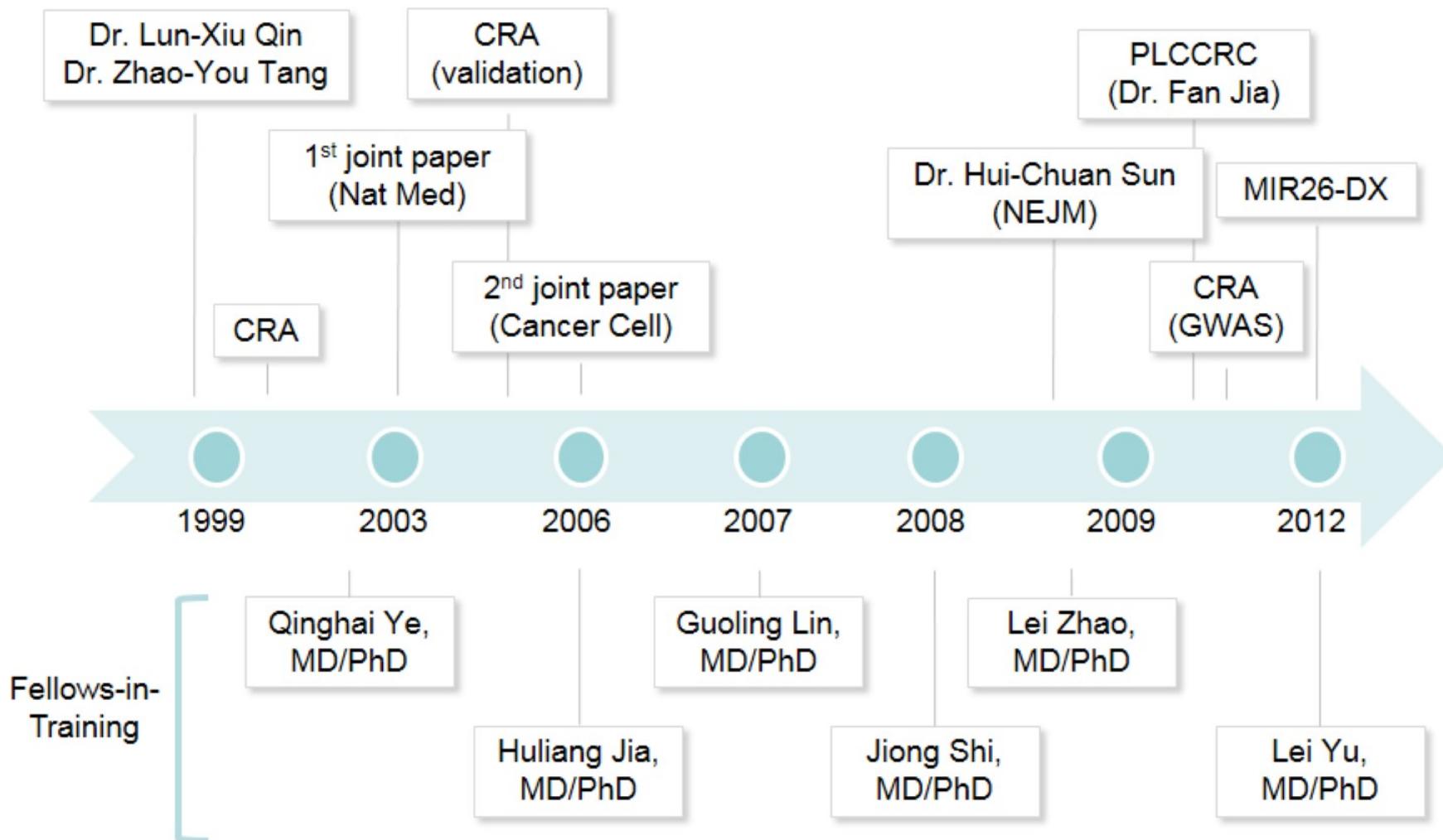
(Collaboration between NCI and Fudan University)



Initiation

Development

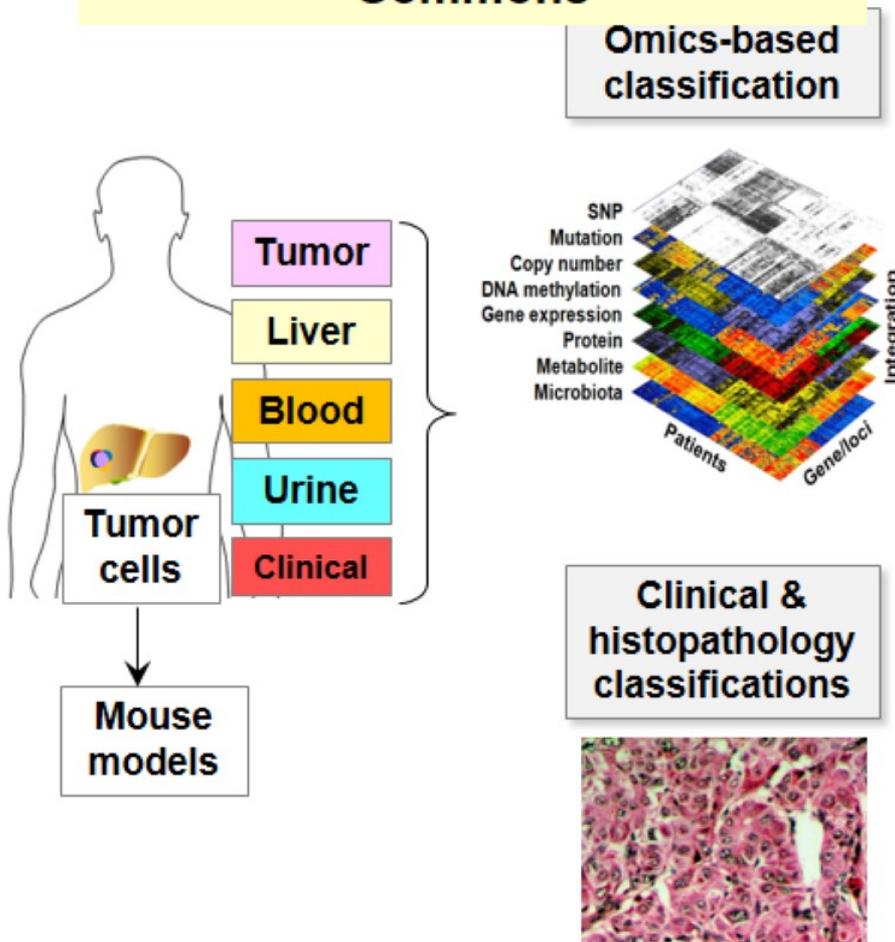
Growth



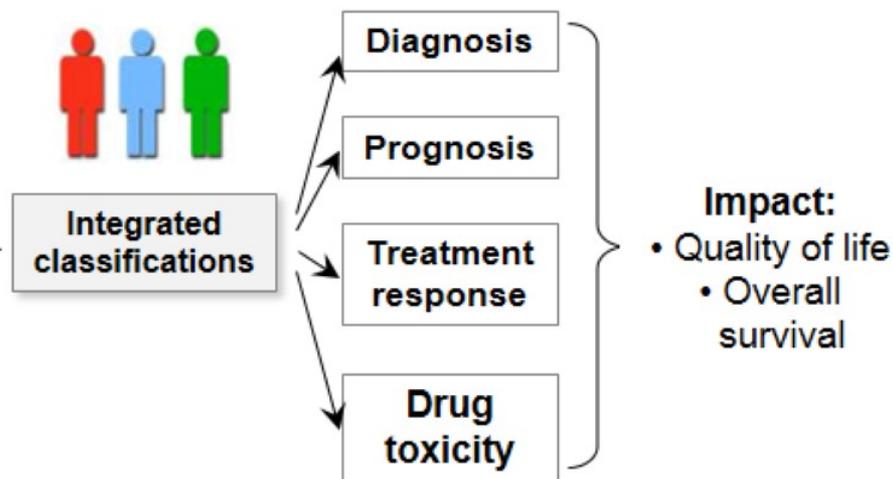
A Systems Biology Strategy to Improve Outcome for Liver Cancer Patients



Biobank & Information Commons



Biomarker-guided Interventions





Major Accomplishments

- **A molecular signature predictive of HCC metastasis and relapse in early stage tumors** (*Ye et al, Nat Med 2003; Roessler et al, Cancer Res 2010*)
 - Established proof of concept that the ability to metastasize may be an inherent quality of the primary tumor; a HeproDX test by GoPath Laboratories
- **A unique immune response signature of the liver microenvironment is predictive of HCC metastasis** (*Budhu et al, Cancer Cell 2006*)
 - Solidified the contribution of the tumor stroma to HCC progression
- **A gender-related HCC biomarker (miR-26) predicts response to interferon therapy** (*Ji et al, N Engl J Med 2009*)
 - Identified a clinically relevant predictive HCC biomarker; developed a miRNA-26 companion diagnostic test used in concert with a multi-center RCT (NCT01681446)
- **Integrated genomics of HCC** (*Roessler et al, Gastroenterology 2012; Oishi et al, Hepatology 2013; Budhu et al, Gastroenterology 2013*)
 - Molecular and bioinformatics strategies to define HCC subtypes and driver genes (potential optimal druggable targets)

Collaborative Studies Between NCI and Fudan University (1999-2015)



- **>20 joint Peer-reviewed publications**
 - Cancer Cell (1)
 - Cancer Res (2)
 - Hepatology (4)
 - Gastroenterology (3)
 - Nat Med (1)
 - N Eng J Med (1)
 - J Hepatology (1)

- **Inventions:** 7 U.S. and/or international patents/applications

- **Awards**
 - Two NSFC grants to Fudan University
 - 2008 Natural Sciences Award (1st place), MOE



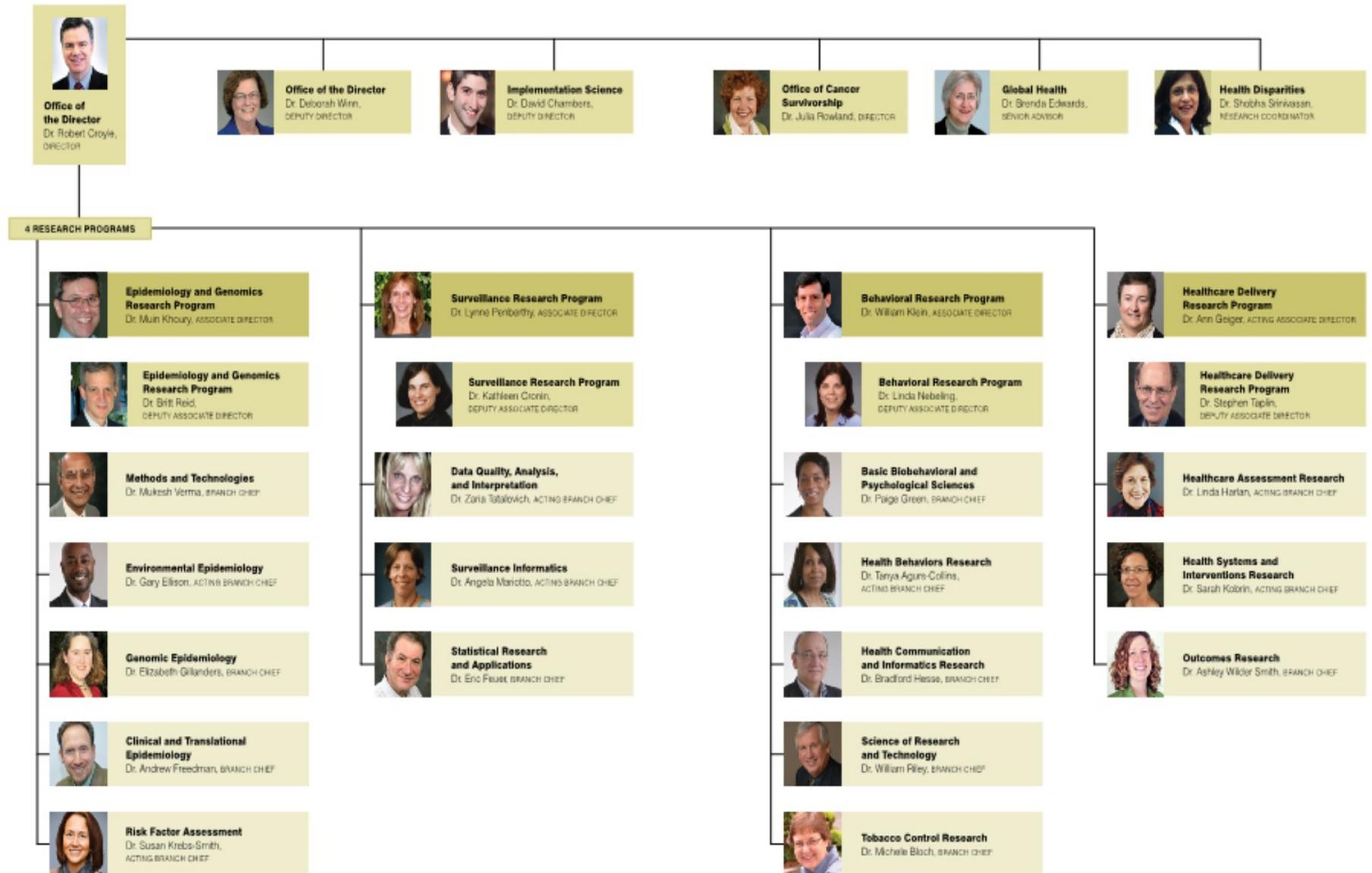
Challenges & Unanswered Questions

- **Better define tumor molecular subtypes:** the liver cancer genome is highly complex; each tumor type contains hundreds of somatic alterations along with alterations of complex liver milieu; a need to consolidate molecular signatures and integrate data from multiple 'omics' platforms to define key cancer drivers
- **Translate research findings to the clinic:** the presence of considerable genomic alterations constitutes a bottleneck to effectively rank, triage and evaluate key cancer drivers as druggable targets; a need to develop precision models that incorporate both genomic changes in tumor cells and the appropriate liver milieu; clinically relevant biomarkers of therapeutic response needed; immune therapy
- **The role of less-studied risk factors:** dietary factors, lifestyle factors, liver fluke, etc.
- **Health disparities and global health:** understudied populations and comparisons
- **Group/Collaborative efforts:** Bench/Clinical/Multi-Institutional collaborations; NCI-Sponsored liver consortium and well-defined epidemiology/population studies
- **Lack of funding/resources for liver-related research and biobanks/repositories**

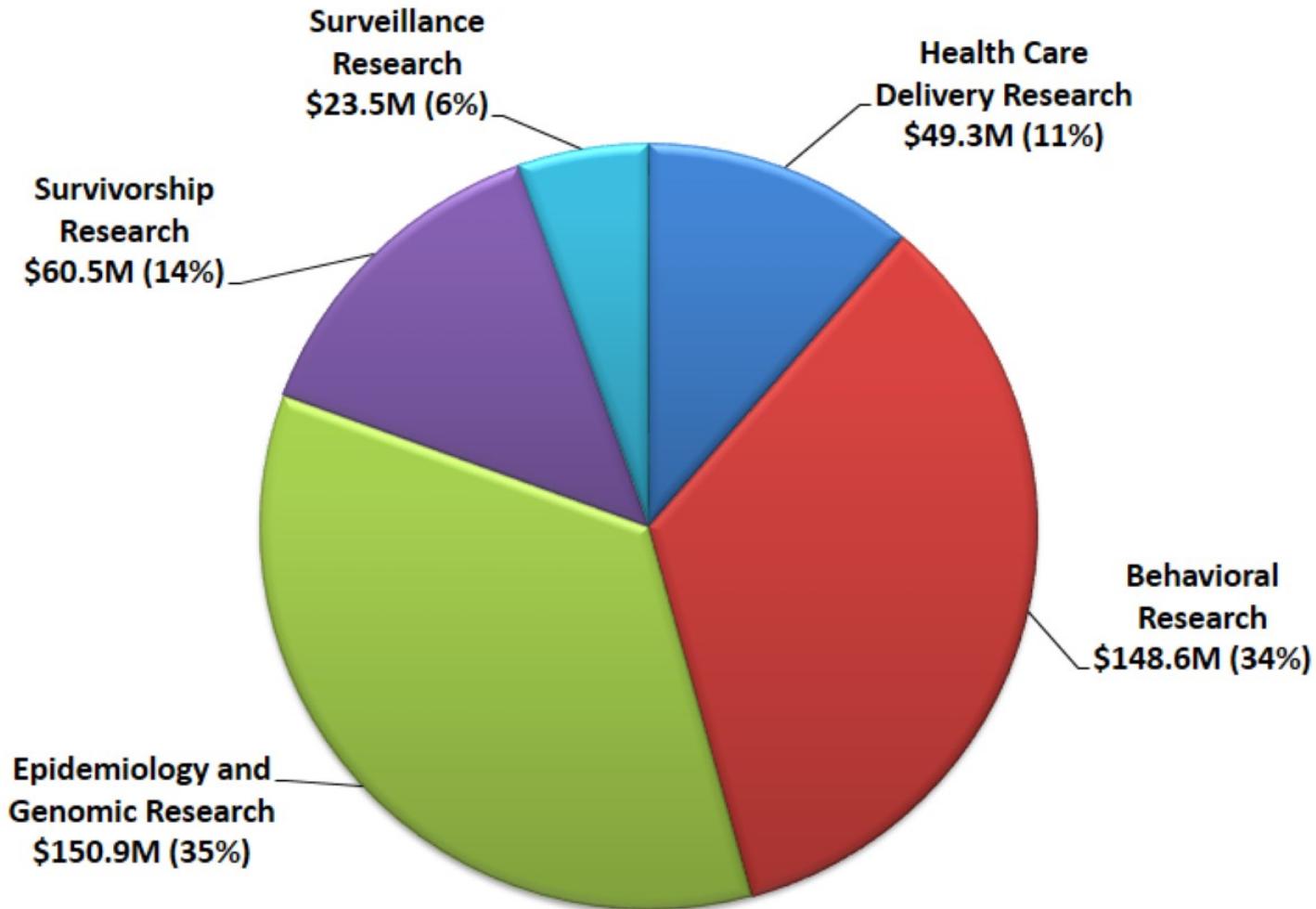
Overview of the Division of Cancer Control and Population Sciences

Robert T. Croyle, PhD
Director

DCCPS Organization – FY 2015



DCCPS FY14 Grant Portfolio Funding



Overview of selected DCCPS – China Research Activities

*Convening, collaborating, and funding to
reduce cancer burden*

Britt Reid, PhD

Division of Cancer Control and Population Sciences

Mutual Scientific Interests

- Environmental exposures in cancer risk
 - Includes diet, nutrition, physical, chemical, and infectious agents
- Genetic variance in cancer risk
 - Includes epigenetic variance
- Tobacco Control
 - Includes policy interventions, behavior change

Studies of Genetic Variance and Environmental Exposures

- DCCPS currently funds 31 individual grants or cooperative agreements among Chinese populations
 - Combined total costs of \$18.3M annually
 - Combined total enrolment of over 226,000 Chinese participants
- Outcomes include: Incidence of breast, colon, prostate, gynecologic, lymphoma, gastric, and lung cancers

Critical Cohorts for Discovery

1. Shanghai Women's Health Study
 - 61,850
 - 2001 - present
2. Shanghai Men's Health Study
 - 75,220
 - 1996 - present
3. Shanghai/Singapore Cohort
 - 81,500
 - Shanghai Health Study – 1987 - 2010;
 - Singapore Cohort Study – 1999 -2010;
 - The two cohorts were combined in 2010

Shanghai Women's Health Study (SWHS)

- Established 1996, N=75,000. PI – Wei Zheng
 - Over 5,000 incident cases identified by the Shanghai Cancer Registry
 - 90% of study participants provided blood, urine and buccal cell samples at baseline; tumor tissue for 70% of cancer cases
 - Repeated measures of exposures over years, 92% response rate
 - Over 200 manuscripts published, 80 studies supported, 50 junior investigators/postdoctoral fellows mentored
 - SWHS resources used in over 20 GWAS, including glioma, pancreas, esophagus, stomach, ovary, and liver cancers

Shanghai Women's Health Study (SWHS)

- SWHS investigators identified 7 novel susceptibility loci/risk variants for breast cancer, first locus for ER-negative breast cancer (Nature Genetics, 2009)
 - HZ 60% elevated risk of breast cancer
- SWHS investigators established the Asia Colorectal Cancer Consortium
 - 12 groups, over 13,000 cases/controls, found 3 novel risk loci for CRC (Nature Genetics, 2012)
 - Asian Cohort Consortium including SWHS investigators, 1M subjects from 19 cohorts, found a U-shaped association between BMI and cause-specific mortality (NEJM, 2011)
 - Protective effect shown for soy-food intake with breast cancer risk among premenopausal women (Am J Clin Nutr, 2009)

Consortia with Chinese populations

- Ability to study rare cancers and exposures by pooling data
- Ability to establish common data elements and protocols
- Ability to share expertise
- EGRP provides portal, scientific liaison, and best practices
- 15 consortia include Chinese populations
 - wide range of cancers and exposures
 - Over last 5 years these consortia have submitted 26 grant applications, 15 of which were funded

Extent and Range of Relevant Consortia

- 1) Asia Cohort Consortium (ACC)
- 2) Asian Breast Cancer Consortium
- 3) Asian Colorectal Cancer Consortium
- 4) Asian Barrett's Consortium
- 5) Breast Cancer Association Consortium (BCAC)
- 6) Breast Cancer Consortium for Outcomes and Survival (BC2OS)
- 7) Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO)
- 8) The Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA)
- 9) Epidemiology of Endometrial Cancer Consortium (E2C2)
- 10) Genetic Associations and Mechanisms in Oncology (GAME-ON)
- 11) International Consortium for Investigation of Inherited Renal Malignancies (I-ConFIRM)
- 12) International Consortium of Bladder Cancer (ICBC)
- 13) International Lung Cancer Consortium (ILCCO)
- 14) Ovarian Cancer Association Consortium (OCAC)
- 15) Pancreatic Cancer Case Control Consortium (PANC4)

Collaboration for Tobacco Control

mHealth Projects

DCCPS and Chinese partners test mHealth tools for smoking cessation

- RCT of a text-message-based smoking cessation intervention
- RCT of strategies to reduce secondhand smoke exposure among infants

HINTS China (sponsored by China's Ministry of Health)

DCCPS technical support and analyses for the Health Information National Trends Survey (HINTS) in China

China-US Smokefree Workplace Partnership

Public-private partnership to promote smokefree workplaces

Workshops and Technical Assistance

Joint workshops and ongoing scientific exchange in tobacco control research with China CDC, the Chinese Academy of Medical Sciences, Peking University Medical College, WHO China Office, and other partners

Future Opportunities to Collaborate

- Top DCCPS Scientific Priorities
 - Health Disparities:
 - Differences in risk and occurrence
 - Survivorship:
 - Current lack of Asian survivorship cohorts
 - Implementation and Dissemination:
 - Translation of risk predictors into interventions

DCEG Studies in China

Stephen J. Chanock, M.D.

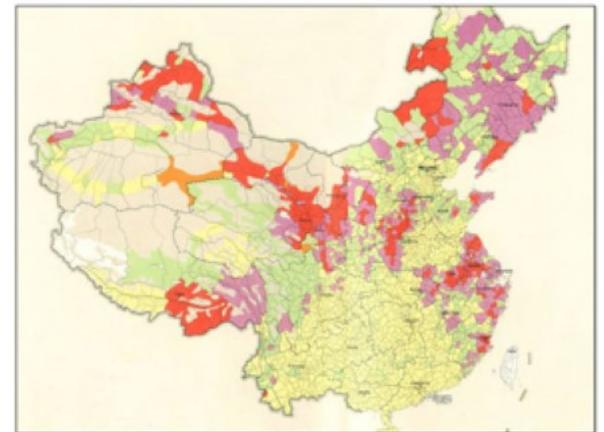
Christian C. Abnet, Ph.D.

Division of Cancer Epidemiology and Genetics

June 24, 2015

DCEG Studies in China

- More than 30 years collaboration
 - Currently over 25 studies
- Insights from cancer maps led to epidemiologic field studies
 - Unusual patterns of risk for lung, esophagus, and stomach cancer
- Unique opportunities to study occupational exposures



Chinese Collaborators



DCEG Trainees in China



DCEG Studies in China: Special Exposures

- Occupational exposures

Shanghai, Tianjin

- Benzene
- Formaldehyde
- Trichloroethylene
- Particulates: diesel exhaust and coal combustion products



- Physical activity

Shanghai

DCEG Studies in China: Lung Cancer

- Lung cancer among never-smoking women

Shanghai, Shenyang, Xuanwei

- Indoor air pollution from coal used for cooking
- Identified risks
- Intervention by ventilating stoves
- Lung cancer rates decreased substantially



- Residential radon from underground dwellings

Shenyang



Consortium to Study Environmental and Genetic Etiology of Lung Cancer in Never-Smoking Females

- Genome-wide Association Study
 - ~13,000 cases from 19 studies
- 8 Novel Signals
 - Majority unique to non-smokers
 - No association found at 15q25.1
 - 2 gene-environment interactions with indoor use of coal for heating/cooking
- Ongoing Exome Sequencing
 - Susceptibility study
 - Tumor/Normal pairs
- Link residential histories to air pollution databases and satellite data



● Study sites

Combined GWAS of Esophageal Squamous Carcinoma

- Call for Data Sharing
 - Published editorial in *Nature Genetics* 2011
 - Based 3 parallel papers for ESCC
- Pooled, combined analysis
 - Individual data exchange
 - New loci
 - Correction of 4 previously published

nature
genetics

Corrigendum: Genome-wide association analyses of esophageal squamous cell carcinoma in Chinese identify multiple susceptibility loci and gene-environment interactions

nature
genetics

Wu, et al. 46:1001-1006, 2014

Joint analysis of three genome-wide association studies of esophageal squamous cell carcinoma in Chinese populations

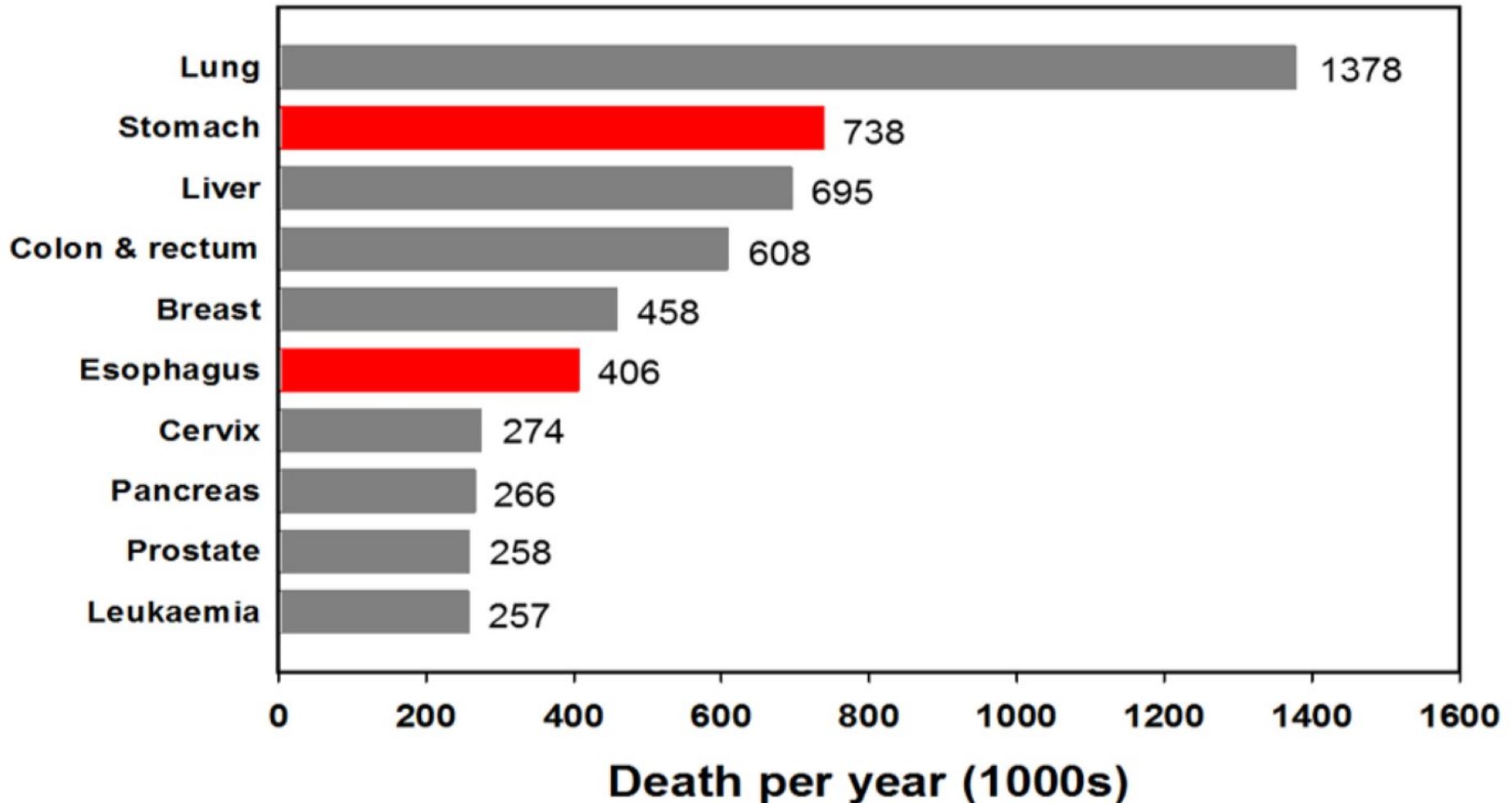
Chen Wu^{1,63}, Zhaoming Wang^{2,3,63}, Xin Song^{4,5,63}, Xiao-Shan Feng^{6,63}, Christian C Abnet^{2,63}, Jie He^{7,63}, Nan Hu^{2,63}, Xian-Bo Zuo^{8,63}, Wen Tan^{1,63}, Qimin Zhan¹, Zhibin Hu⁹, Zhonghu He¹⁰, Weihua Jia^{11,12}, Yifeng Zhou¹³, Kai Yu², Xiao-Ou Shu^{14,15}, Jian-Min Yuan¹⁶, Wei Zheng^{14,15}, Xue-Ke Zhao⁵, She-Gan Gao⁶, Zhi-Qing Yuan¹, Fu-You Zhou¹⁷, Zong-Min Fan⁵, Ji-Li Cui^{4,5}, Hong-Li Lin^{4,5}, Xue-Na Han⁵, Bei Li⁵, Xi Chen^{5,18}, Sanford M Dawsey², Linda Liao², Maxwell P Lee¹⁹, Ti Ding²⁰, You-Lin Qiao²¹, Zhihua Liu¹, Yu Liu¹, Dianke Yu¹, Jiang Chang¹, Lixuan Wei¹, Yu-Tang Gao²², Woon-Puay Koh²³, Yong-Bing Xiang²², Ze-Zhong Tang²⁰, Jin-Hu Fan²¹, Jing-Jing Han^{5,18}, Sheng-Li Zhou⁵, Peng Zhang⁵, Dong-Yun Zhang⁵, Yuan Yuan⁵, Ying Huang¹, Chunling Liu¹, Kan Zhai¹, Yan Qiao¹, Guangfu Jin⁹, Chuanhai Guo¹⁰, Jianhua Fu^{11,12}, Xiaoping Miao²⁴, Changdong Lu¹⁷, Haijun Yang¹⁷, Chaoyu Wang², William A Wheeler²⁵, Mitchell Gail², Meredith Yeager^{2,3}, Jeff Yuenger^{2,3}, Er-Tao Guo⁵, Ai-Li Li^{5,26}, Wei Zhang⁵, Xue-Min Li²⁷, Liang-Dan Sun⁶, Bao-Gen Ma²⁸⁻³⁰, Yan Li⁵, Sa Tang⁵, Xiu-Qing Peng^{5,6}, Jing Liu⁵, Amy Hutchinson^{2,3}, Kevin Jacobs^{2,3}, Carol Giffen²⁵, Laurie Burdette^{2,3}, Joseph F Fraumeni Jr², Hongbing Shen⁹, Yang Ke¹⁰, Yixin Zeng^{11,12}, Tangchun Wu²⁴, Peter Kraft³¹, Charles C Chung^{2,3}, Margaret A Tucker², Zhi-Chao Hou⁵, Ya-Li Liu^{4,5}, Yan-Long Hu^{4,5}, Yu Liu⁹, Li Wang^{4,32}, Guo Yuan^{4,5}, Li-Sha Chen^{4,5}, Xiao Liu⁹, Teng Ma⁵, Hui Meng⁵, Li Sun⁵, Xin-Min Li⁵, Xiu-Min Li⁴, Jian-Wei Ku^{5,33}, Ying-Fa Zhou^{5,31}, Liu-Qin Yang³⁴, Zhou Wang³⁵, Yin Li³⁶, Qiren Wang³⁷, Wen-Jun Yang³⁸, Guang-Yan Lei³⁹, Long-Qi Chen⁴⁰, En-Min Li^{41,42}, Ling Yuan³⁶, Wen-Bin Yue^{5,43}, Ran Wang⁵, Lu-Wen Wang⁵, Xue-Ping Fan⁵, Fang-Heng Zhu³⁴, Wei-Xing Zhao⁴, Yi-Min Mao⁶, Mei Zhang⁵, Guo-Lan Xing⁵, Ji-Lin Li⁴⁴, Min Han⁴⁵, Jing-Li Ren³², Bin Liu⁴⁶, Shu-Wei Ren⁴⁷, Qing-Peng Kong⁴⁸, Feng Li⁴⁹, Ilyar Sheyhidin^{50,51}, Wu Wei^{52,53}, Yan-Rui Zhang²⁸⁻³⁰, Chang-Wei Feng³², Jin Wang⁵, Yu-Hua Yang⁵⁴, Hong-Zhang Hao⁵⁵, Qi-De Bao⁵⁵, Bao-Chi Liu⁵⁶, Ai-Qun Wu⁵⁷, Dong Xie⁵⁸, Wan-Cai Yang⁴, Liang Wang^{4,59}, Xiao-Hang Zhao⁶⁰, Shu-Qing Chen⁶¹, Jun-Yan Hong^{61,62}, Xue-Jun Zhang⁸, Neal D Freedman², Alisa M Goldstein², Dongxin Lin¹, Philip R Taylor², Li-Dong Wang^{4,5} & Stephen J Chanock²

nature
genetics

Corrigendum: Genome-wide association study of esophageal squamous cell carcinoma in Chinese subjects identifies susceptibility loci at *PLCE1* and *C20orf54*



Worldwide Ranks of Cancer Mortality



DCEG Studies in China: Upper Gastrointestinal Cancers

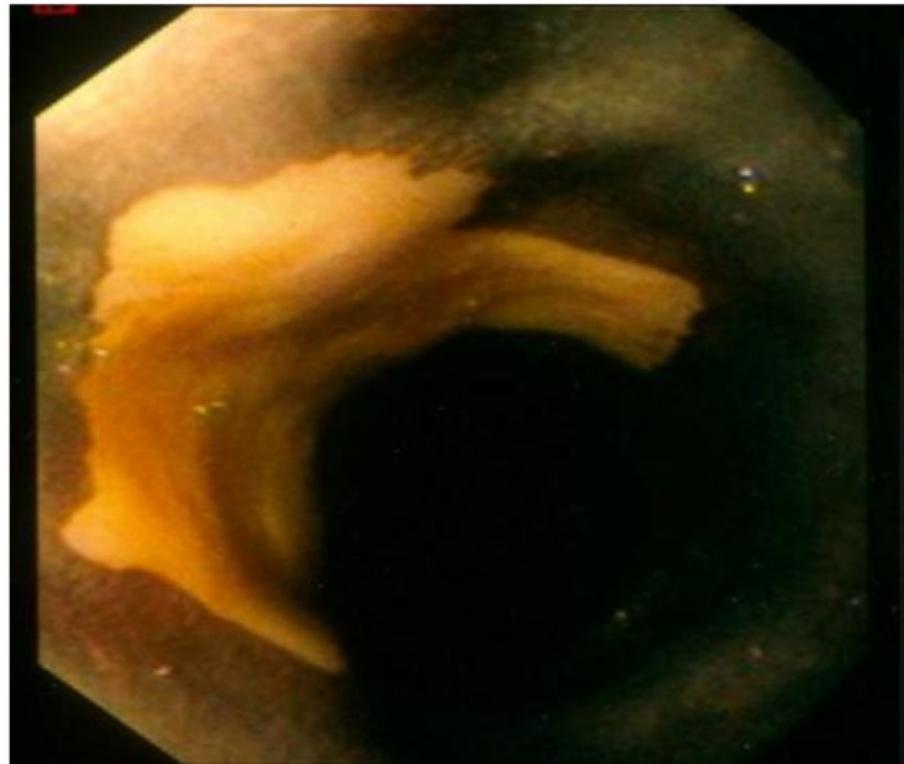
- **Nutrition Intervention Trials in Linxian, Henan**
 - Early detection of esophageal cancer
- ***H. pylori* treatment trial in Linqu, Shandong**
- **Genome-wide association studies**
- **Tooth loss & oral hygiene → microbiome**
 - Yunnan Tin Miner's Cohort with serial sputum samples



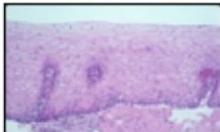
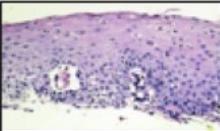
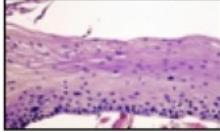
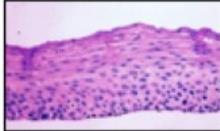
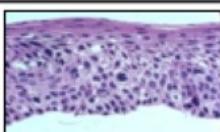
General Population NIT: Summary of Significant Trial Results

- **Selenium, β -carotene, and vitamin E**
 - Total mortality reduced 9%
 - Total cancer mortality reduced 13%
 - Total gastric cancer mortality reduced 21%
- **32,912 subjects being followed**
 - 6,332 incident UGI cancer cases
 - Observational studies
 - >100 publications
 - Serum selenium and UGI cancer risk
 - HPV and esophageal cancer risk

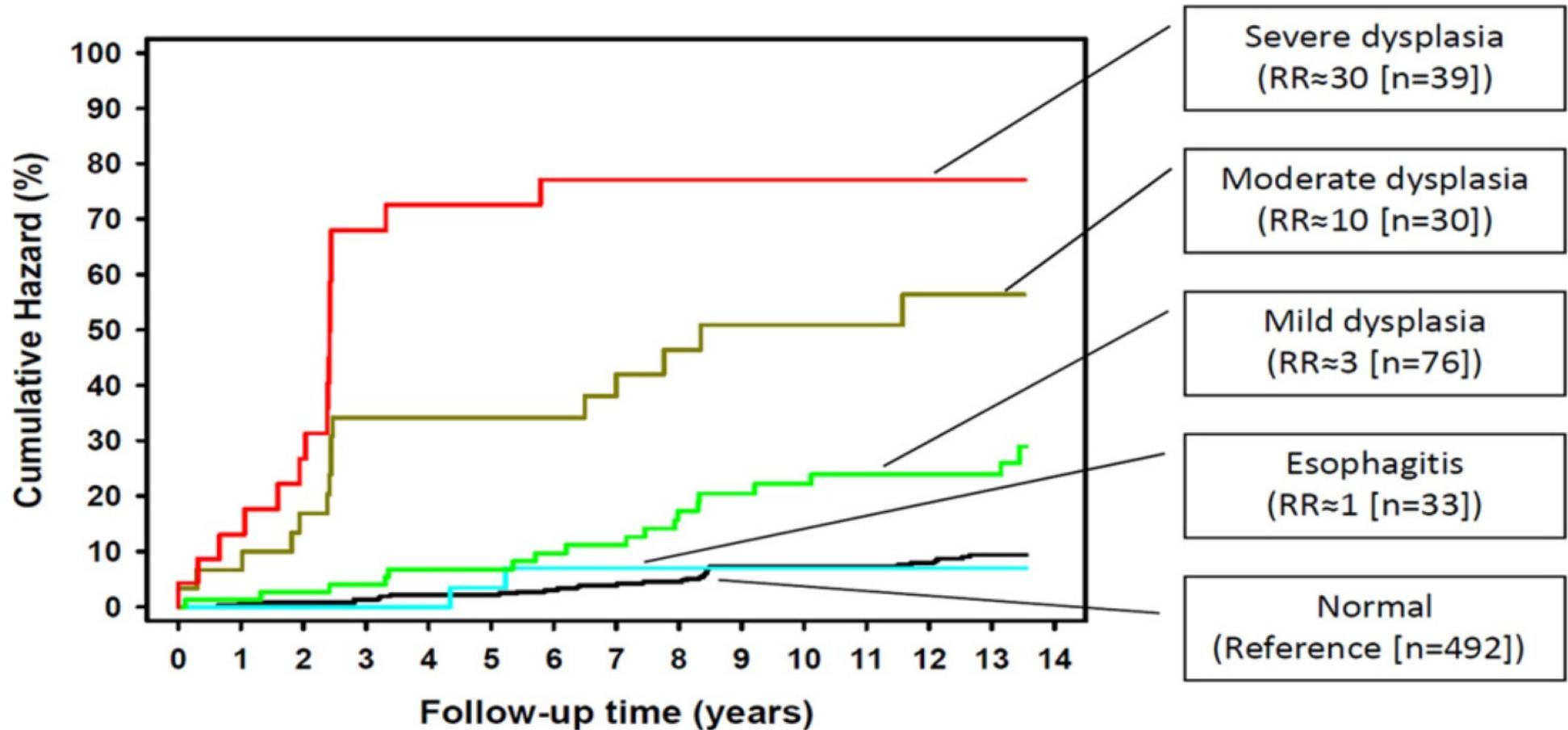
Early Detection and Intervention



Endoscopic Localization with Lugol's

Diagnosis		Sensitivity of Unstained Lesions
Normal		---
Esophagitis		---
Mild Dysplasia		63%
Moderate Dysplasia		93%
Severe Dysplasia		96%

Squamous Dysplasia is the Precursor



Components of Screening Program

Component	Complete
ID of precursor lesions	✓
Primary screen	✓
Endoscopic localization	✓
Staging	✓
Therapy	✓

Implementation of the Screening Program

VOLUME 33 · NUMBER 17 · JUNE 10 2015

JOURNAL OF CLINICAL ONCOLOGY

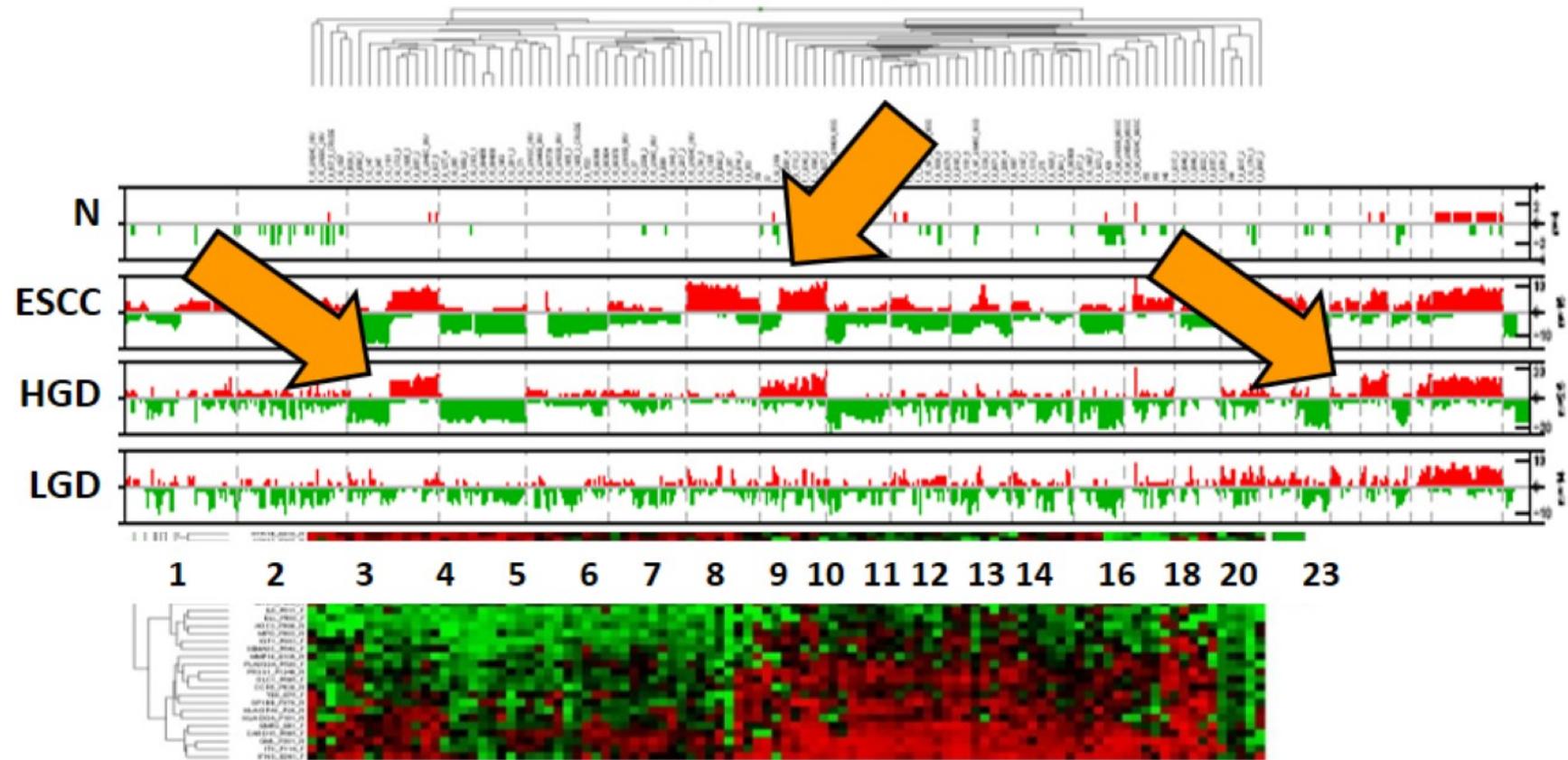
ORIGINAL REPORT

Long-Term Follow-Up of a Community Assignment, One-Time Endoscopic Screening Study of Esophageal Cancer in China

Wen-Qiang Wei, Zhi-Feng Chen, Yu-Tong He, Hao Feng, Jun Hou, Dong-Mei Lin, Xin-Qing Li, Cui-Lan Guo, Shao-Sen Li, Guo-Qing Wang, Zhi-Wei Dong, Christian C. Abnet, and You-Lin Qiao

- **34% reduction in ESCC mortality**

Improved Primary Screening



A

B



Division of Cancer Prevention: Collaborations with China

Joint Meeting of the National Cancer Advisory Board
and the Board of Scientific Advisors

*Barry Kramer, MD, MPH,
Director, NCI Division of Cancer Prevention*

Primary Collaborations with China

- Cancer Screening Trial Feasibility Study
- China Early Detection Research Network
- Chinese Translation of the PDQ Database

Primary Collaborators:

- *National Institute/Hospital of Chinese Academy of Medical Sciences, National Cancer Center (CICAMS, NCC)*
- *DCP serving in an advisory capacity, providing consultation and technical support*
- *NCI Office of Communications and Public Liaison*

China Cancer Screening Trial Feasibility Study

- Lung and colorectal cancer screening
- Confirm NLST results in Chinese urban population
- Practicability of population-based screening for colorectal cancer in China
- Feasibility study for a long-term randomized 3-arm screening trial

Feasibility Study Design

- 3 Cities in Urban China (socioeconomic status)
Hangzhou (high), Changsha (middle), Lanzhou (low)
- 3 Study Arms (2700 participants; 900 in each center)
 - 1) Helical chest CT exam annually + one-time colonoscopy
 - 2) Helical chest CT biennially + OC-FIT for colon cancer annually
 - 3) Septin9 + InSureFIT for colon cancer annually

Study Timeline

- May 2013: Memorandum of Understanding signed
- June 2014: China IRB study approval
- Sep 2014: Began recruitment/enrollment
- Sep 2014 - Mar 2015: T₀ Baseline screenings
- Aug - Dec 2015: T₁ screenings
- Aug - Dec 2016: T₂ screenings

Center Recruitment by Province (*Main City*)

	Gansu <i>Lanzhou</i> (lower SES)	Hunan <i>Changsha</i> (middle SES)	Zhejiang <i>Hangzhou</i> (higher SES)	TOTAL
Invited	11,231	8,000	1,500	20,731
Eligible	4,680	1,500	1,003	7,183
Randomized	900	904	900	2,704

LDCT Screening Preliminary Data (April 15, 2015, by Province, *Main City*)

	Gansu <i>Lanzhou</i>	Hunan <i>Changsha</i>	Zhejiang <i>Hangzhou</i>
# Screened	543	519	542
CT Lung Abnormality			
Yes	436 (80.3%)	469 (90.4%)	336 (62.0%)
No	107 (19.7%)	50 (9.6%)	206 (38.0%)
Non-calcified Nodule/Mass			
<4mm	0 (0.0%)	87 (18.6%)	53 (15.8%)
≥4mm	14 (3.2%)	36 (7.7%)	47 (14.0%)

China Early Detection Research Network (China-EDRN)

- China's leadership interest in establishing an EDRN infrastructure to meet China's needs
- Joint monthly U.S.-China conference calls
- US-EDRN informatics center (Jet Propulsion Laboratory) assisting in establishing China databases
- Collaborative research opportunities with China-EDRN investigators
- China Visiting Scientist at NCI, Apr-Oct 2015

Chinese Translation of the PDQ Database

- Collaboration with NCI's Office of Communications and Public Liaison
- Extending the reach of PDQ cancer information to the Chinese-speaking health professionals
- Pilot phase: Health professional summaries and supporting documents for six cancer types of highest public health interest in China
- Translation and review by content experts completed May 2015
- Construction of website underway



**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol

The Impact of Research Collaboration with NCI

Wang Yu
China CDC
2015, Washington

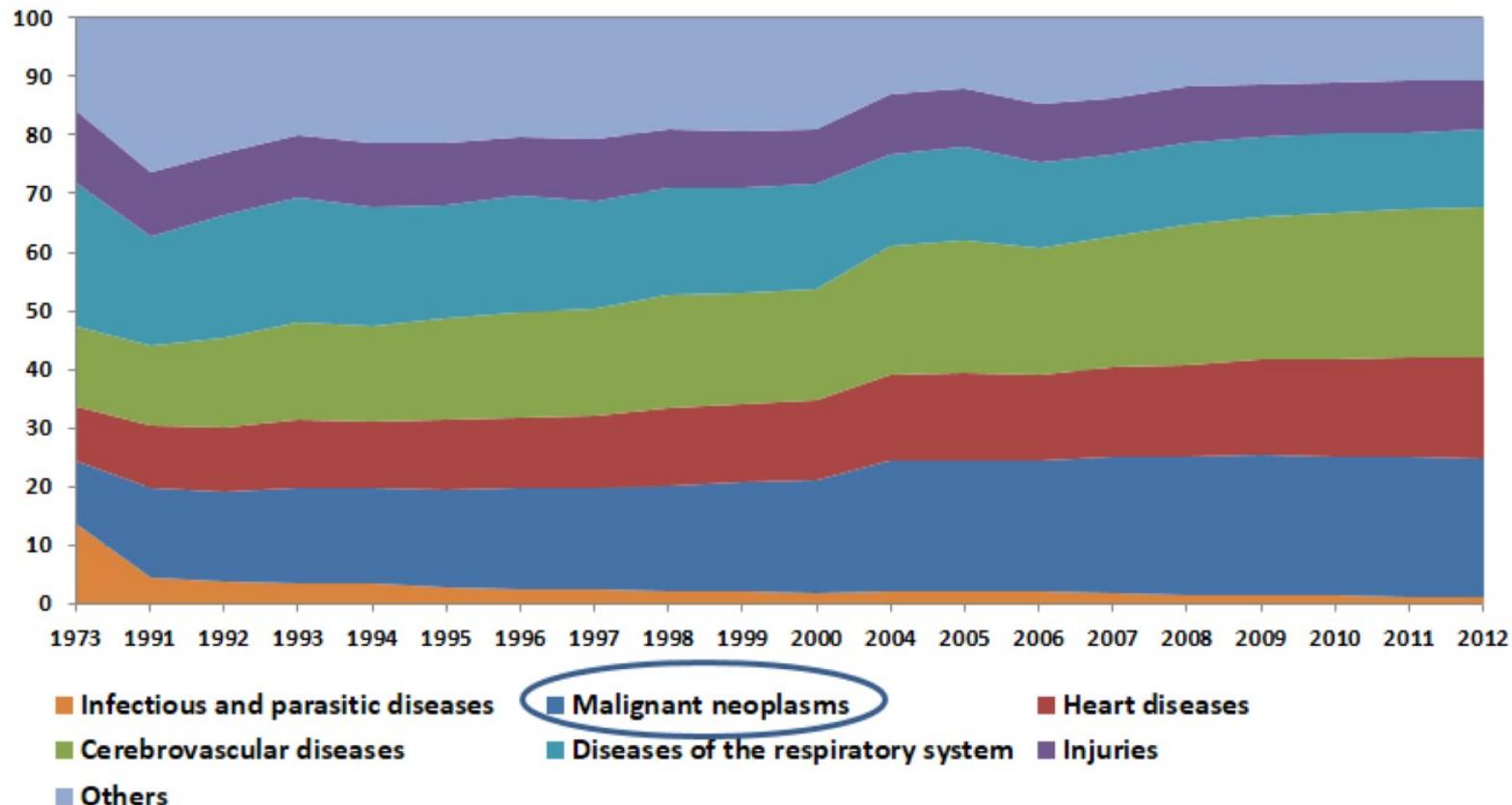


CONTENTS

- ***Cancer Mortality , Prevention & Control in China***
- ***Cancer Risks in Chinese Benzene Workers***
- ***Chinese Children and Families Cohort Study***
- ***The Impact of Collaborations on Cancer Research and Programs in China***
- ***Areas for Future Collaboration***

***Part I. Cancer Mortality, Prevention &
Control in China***

Transition of Causes of Death in China, 1973-2012



Major Causes of Death in China, 2012

Rank	Disease	Mortality (per 100,000)	Percentage of total deaths (%)
1	Cerebrovascular diseases	175.1	25.7
2	Malignant neoplasms	161.7	23.7
3	Heart diseases	116.8	17.1
4	Diseases of the respiratory system	90.5	13.2
5	Injuries	57.5	8.4
6	Diseases of the digestive system	15.7	2.3
7	Endocrine, nutritional and metabolic diseases	13.8	2.0
8	Diseases of the genitourinary system	7.6	1.1
9	Infectious diseases	7.5	1.1
10	Diseases of the nervous system	6.6	1.0

Source: Wang Y, et al. The Annual Report of National Disease Surveillance in 2012.

Cancer-specific Mortality in China, 2012

Cancer ^a	Surveillance mortality by DSPs ^{b,1}				Estimated mortality in GLOBOCAN ^{c,2}
	All areas	Eastern areas	Middle areas	Western areas	All areas
All cancers excl. non-melanoma skin cancer	161.7	174.7	163.9	139.6	162.0
Lung	44.5	50.2	45.1	35.1	43.9
Liver	27.9	27.1	29.3	27.4	28.1
Stomach	22.9	23.6	24.9	19.2	23.9
Esophagus	13.6	13.5	14.0	13.1	14.5
Colorectum	10.1	12.0	9.3	8.3	10.2
Leukaemia	4.1	4.3	4.0	4.0	4.0
Breast	3.7	4.1	3.8	2.8	7.3
Nasopharynx	1.8	1.9	1.5	2.0	1.5
Bladder	1.7	2.0	1.7	1.1	2.0
Cervix uteri	1.7	1.4	2.0	1.6	4.5

^a. Ordered by the top 10 cancer surveyed by Disease Surveillance Points.

^b. Crude rate, per 100,000. Excluding Hong Kong and Macao.

^c. Crude rate, per 100,000. Including Hong Kong and Macao.

Source: 1. Wang Y, et al. The Annual Report of National Disease Surveillance in 2012; 2. GLOBOCAN 2012, IARC.

The Prevention and Control of Cancer in China

- ***Tobacco Control in China***

- ✓ *National Smoke-free Policies and Local Smoke-free Laws*
- ✓ *Notices issued by State Council and Communist Party*
- ✓ *Monitoring and Evaluation*

- ***Cancer Screening Project***

- ✓ *Early detection and treatment Project*
- ✓ *National “Two cancers” (cervical and breast cancer)*

- ***Vaccine and cancer protection (China’s Successful Story of HBV Vaccination)***

Part II. Cancer Risks in Chinese Benzene Workers

China CDC / U.S. NCI

Background

- **Benzene is used worldwide in chemical manufacturing**
- **Low level exposure is common to the general population in gasoline, motor vehicle exhaust, tobacco smoke**
- **Benzene causes acute myeloid leukemia, aplastic anemia, & reproductive effects at high exposure levels, but risks at low exposures for these & other cancers is poorly understood**
- **More information is needed about genetic susceptibility, biomarkers to identify those at high risk, and other aspects of biological mechanisms**

Results: 1986-2001

- Excesses of a spectrum of hematopoietic diseases (all types of myeloid and lymphoid leukemias, non-Hodgkin lymphoma, aplastic anemia, myelodysplastic syndrome)
- Suggested excess risk at low levels (<10 ppm)
- Dose-response relationship for acute myeloid leukemia and non-Hodgkin lymphoma
- Suggested excess risk of lung cancer
- Evidence of genetic susceptibility
- Identified biomarkers of exposure and of biological effects at low exposure levels

Impact of Research

Results from collaborative China CDC – U.S. NCI studies:

- Formed basis of changing occupational threshold limit values in China**
- Used by U.S. Environmental Protection Agency (EPA) to reconsider basis for allowable environmental levels**

Recent and Ongoing

- **Confirmed excesses of a spectrum of hematopoietic diseases (all types of myeloid and lymphoid leukemias, non-Hodgkin lymphoma, aplastic anemia, myelodysplastic syndrome)**
- **Analyzing dose-response for acute myeloid leukemia, non-Hodgkin lymphoma and lung cancer**
- **Evaluating genetic susceptibility and other biomarkers for benzene hematotoxicity**

***Part III. Chinese Children and
Families Cohort Study (CFCS)***

China CDC / U.S.NCI / U.S. CDC

Background

- **Community intervention project (CIP)**
 - 1993-1995, In 21 field sites of 3 provinces, 240,000 pairs of mothers and offspring
 - A unique population with periconception/early first trimester exposure to folic acid supplements and other periconceptual factors
 - Neural tube birth defect prevalence reduced significantly, Push the policy of folic acid supplement in China
- **CFCS**
 - Prospective cohort follow-up based on the unique CIP population
 - Evaluation possible late health effects of periconceptual folic acid on the risk of chronic diseases of mothers, offspring and next generation in an Asian population
 - China's unique population provides an important opportunity to assess a potential preventive public health measure to reduce risk of chronic diseases.

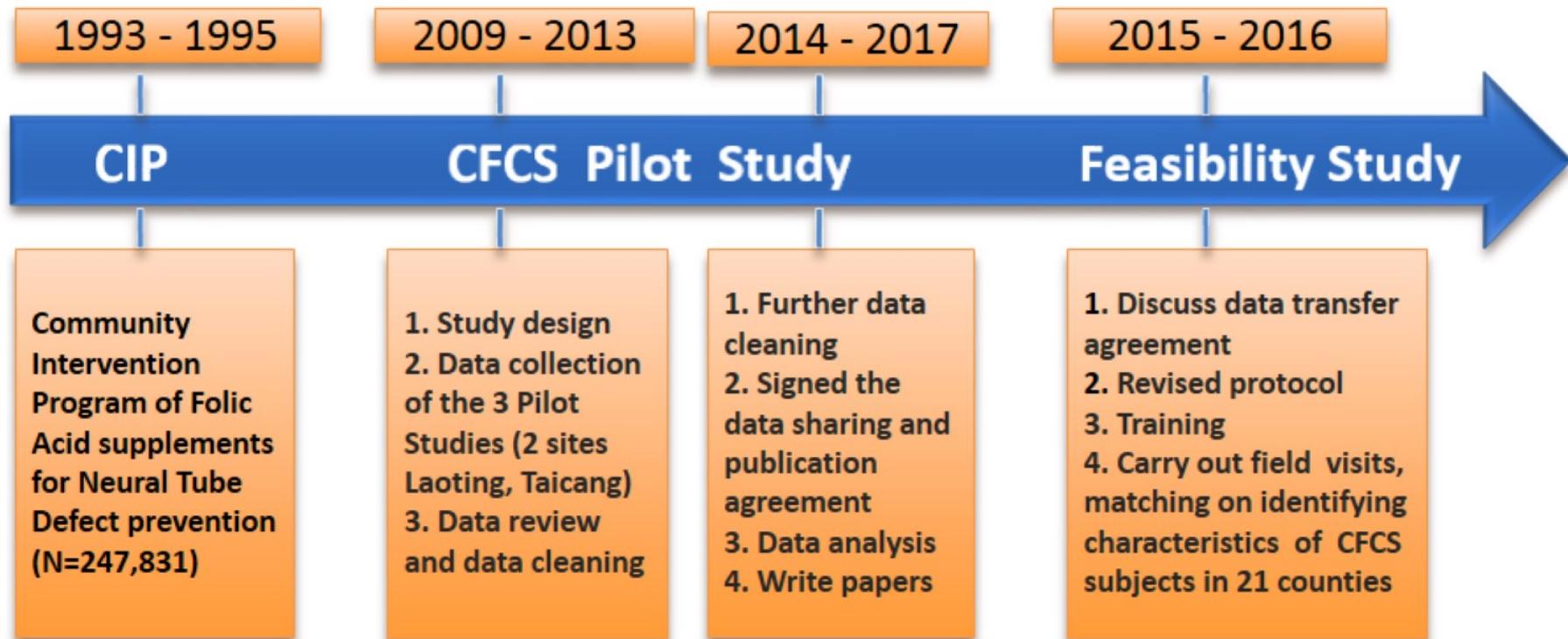
Three Pilot Studies Completed

Study 1: Follow-up of late effects of periconceptional folic acid supplement on CFCS Mothers and their children

Study 2: Assessment of early life and early adulthood risk factors for adult cancers and other chronic diseases (Diet, Nutrition, Physical Activity, Ultraviolet Radiation (UV), and Associated Biomarkers in CFCS Mothers and Offspring)

Study 3: Pediatric cancer cases record linkage cohort & nested case-control study of postulated risk factors for pediatric cancer

Progress on CFCS



Feasibility Study

Specific Aim

- **To determine the feasibility of re-identifying CFCS families on a substantially larger scale than the previous Pilot Study #1**

Study Population

- **CFCS offspring in 5 counties in Hebei Province**
- **CFCS offspring in 16 counties in Jiangsu and Zhejiang Provinces**

Methods

- **Identify databases in the local sites to re-construct cohort**
- **Match with CIP list**

***Part IV. The Impact of NCI
Collaborations on Cancer Research
and Programs in China***

Impact of NCI Collaborations on Cancer Research and Programs in China

- Deepen mutual understanding and trust**
- Strengthen technical exchange and training**
- Provide opportunities for international cooperation and scientific research among young professionals**
- Promote research on the association between periconceptual, prenatal, and childhood exposures and risks of chronic diseases such as cancer**

Part IV. The Areas for Future Collaboration

Areas for Future Collaboration

- Further expand research on the association of early life exposures and chronic diseases such as cancer**
- Enhance the collaborative CFCS data analysis and publication, to provide the scientific basis for prevention of cancer and other chronic diseases**
- Strengthen the cooperation, communication, and training on data collection and management, and analysis of cancer descriptive and analytic studies between China and US**

Areas for Future Collaboration

- Continue to expand cooperation in the field of study of cancer risk factors, for example, the relationship between environment and cancer**
- Enhance research and collaboration on cancer prevention, intervention, and vaccine development and application**

Thank You!

Impact of NCI-China Cancer Research Collaboration from China's perspective



Prof. You-Lin QIAO, MD; PhD et al

**Department of Cancer Epidemiology (DCE)
National Cancer Center
Cancer Institute/Hospital (CI)
Chinese Academy of Medical Sciences (CAMS)
Peking Union Medical College (PUMC)**

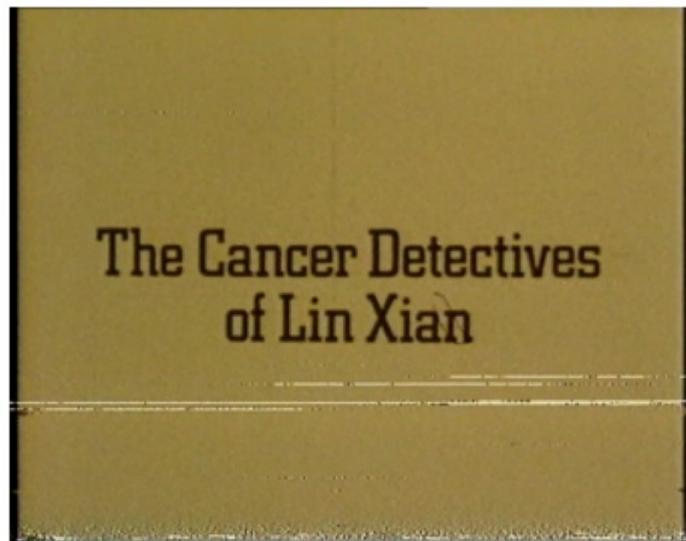
**NCI CGH session at the Joint Meeting of the NCAB/BSA
June 24, 2015**

Outline

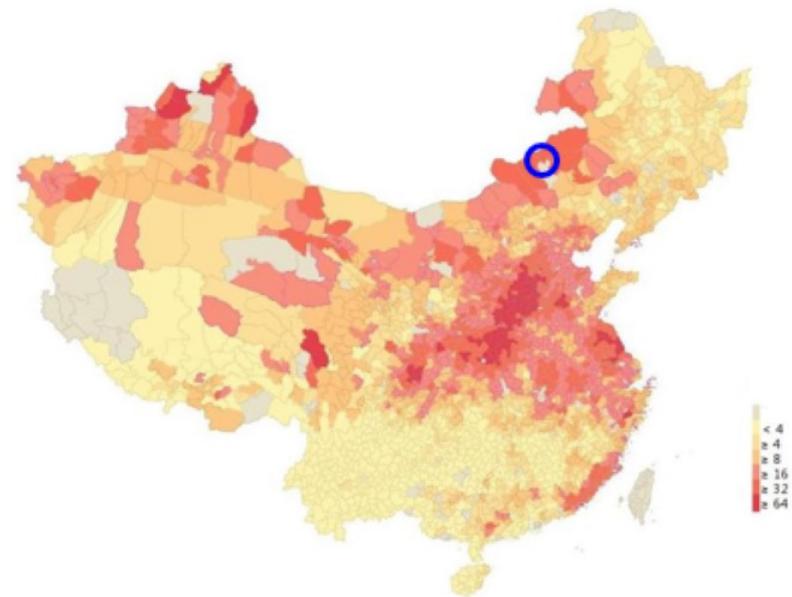
- 1. Brief review of the history of collaborations with NCI**
- 2. Impact of NCI past and current collaborations on cancer research and programs in China**
- 3. Areas for future collaboration with NCI**

1. Brief review of the history of collaborations

Few medical projects can ever have been successfully carried through that compare in scale with national survey of the cause of death undertaken in China in 1975. That immense task, which involved identification of about 20 million deaths... This provided epidemiologists with a unique opportunity for testing hypotheses about the etiology of diseases, and possibly for obtaining some entirely new clues. (R. Doll & P. Greenwald)



BBC documentary 1983



1973-75 China National Mortality Survey

1.1 Epidemiological studies and Nutrition Intervention Trial (NIT)

- 1982, CICAMS submitted NIT proposal to DCE/NCI, and the pilot study approved by Chinese MOH
- 1984, Case-control studies on cancers of esophagus, lung, stomach, and choriocarcinoma (DCE)
- 1985-1991, NIT study and follow-up (DCE/DCPC)
- 1984、1991、1996、1999-2000, Nutrition survey, serum collection (DCE/DCPC)
- 1991-2015, continue follow up until now (DCEG/DCPC)



More etiology Studies (DCEG/DCPC)

1. **Zinc Deficiency & Esophageal Cancer**
2. **Serum selenium, cysteine, Vitamin E, Serum 25(OH)-vitamin D & esophageal squamous dysplasia, esophageal and gastric cancers**
3. **Serum pepsinogens & esophageal squamous dysplasia**
4. **Helicobacter pylori & esophageal and gastric cancers**
5. **HPV infection & esophageal Cancer**
6. **Epidemiological study of HPV & cervical cancer in Shanxi, China**

- Abnet CC, Lai B, Qiao YL, Vogt S, Luo XM, Taylor PR, Dong ZW, Mark S, Dawsey SM. *JNCI*, Feb. 16, 2005, 97(4): 301-306.
- Qu CX, Kamangar F, Fan JH, Yu B, Sun XD, Taylor PR, Chen BE, Abnet CC, Qiao YL, Mark SD, Dawsey SM. *J Natl Cancer Inst.* 2007 ;99(16):1240-7
- Ren JS, Kamangar F, Qiao YL, Taylor PR, Liang H, Dawsey SM, Liu B, Fan JH, Abnet CC. *Serum. Gut.* 2009 May;58(5):636-42.
- Limburg P, Qiao Y, Mark S, Wang G, Perez-Perez G, Blaser M, Wu Y, Zou X, Dong Z, Taylor P, Dawsey S. *J Natl Cancer Inst.* 2001 Feb 7;93(3):226-33.
- Koshiol J, Wei WQ, et al. *Int J Cancer* 2010;127(1):93-100.
- Zhao FH, Forman MR, Belinson J, Shen YH, Graubard BI, Patel AC, Rong SD, Pretorius RG, Qiao YL. *Int J Cancer.* 2006 15;118(2):442-8.

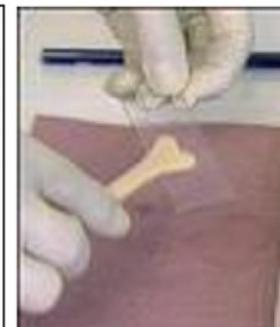
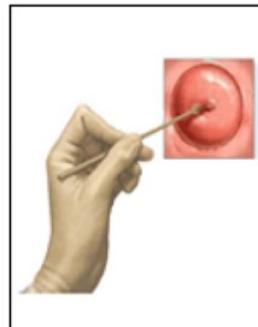


1.2 Early detection of esophageal & cervical cancer & its precancerous lesion research in China (DCPC/DCEG)

- Cytological screening sampling study I & II
- Endoscopy screening method study (iodine staining & biopsy)
- Chemoprevention of esophageal squamous cell carcinoma
- NCC's Upper GI Endoscopy Cohort Studies
- Cervical cancer screening studies



Conventional cytology



HPV DNA tests



A. Balloon Cytology and HPV screening Studies (DCEG)



Fig a, Primary double tubes balloon

Fig b.c Modified single tube balloon

Fig d. Encapsulated sponge cytological samplers

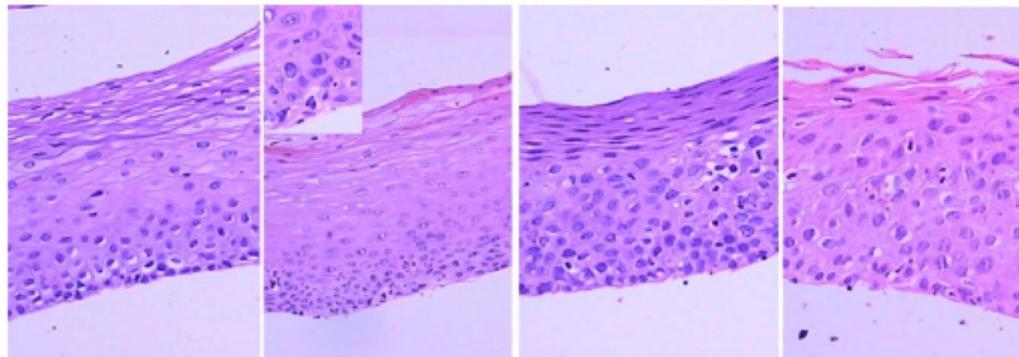
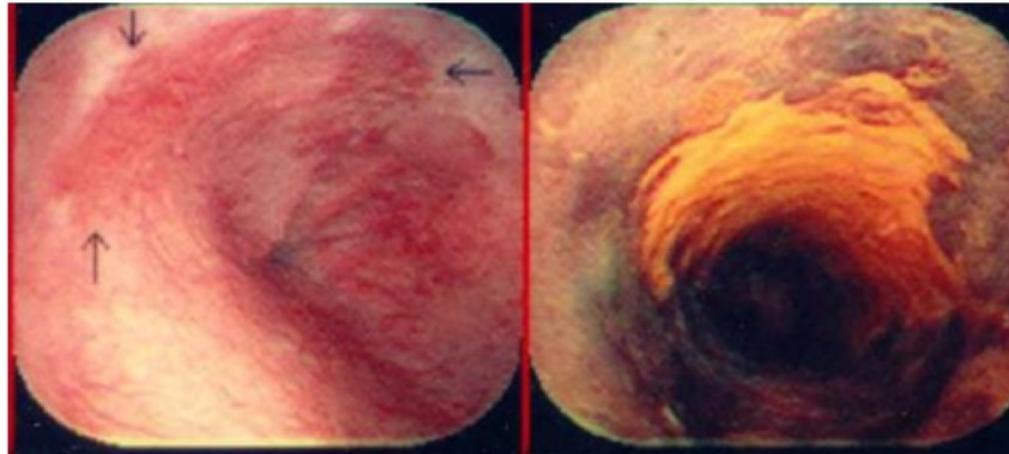
Fig e. Advanced double tubes balloon



(AutoCytte Liquid-Based Preparation)

1. Pan QJ, Roth MJ, Guo HQ, Kochman ML, Wang GQ, Henry M, Wei WQ, Giffen CA, Lu N, Abnet CC, Hao CQ, Taylor PR, Qiao YL, Dawsey SM. Acta Cytol. 2008;52(1):14-23.
2. Dawsey SM, Yu Y, Taylor PR, Li JY, Shen Q, Shu YJ, Liu SF, Zhao HZ, et al. Acta Cytol. 1994 38(2):183-92.
3. Shen O, Liu SF, Dawsey SM, Cao J, Zhou B, Wang DY, Cao SG, Zhao HZ, Li GY, Taylor PR, et al. 993;8;54(2):185-8.
4. Zhao FH, Lin MJ, Chen F, Hu SY, Zhang R, Belinson JL, Sellors JW, Franceschi S, Qiao YL, Castle PE.. Lancet Oncol. 2010 Dec;11(12):1160-1171
5. Zhao FH, Lewkowitz A, Chen F, Lin MJ, Hu SY, Zhang X, Pan QJ, Li CQ, Ma JF, Li SM, Smith JS, Belinson JL, Qiao YL, Castle PE. J Natl Cancer Inst. 2012 Feb 8;104(3):178-88.

B. Endoscopy screening method study (DCEG)



BCH

mD

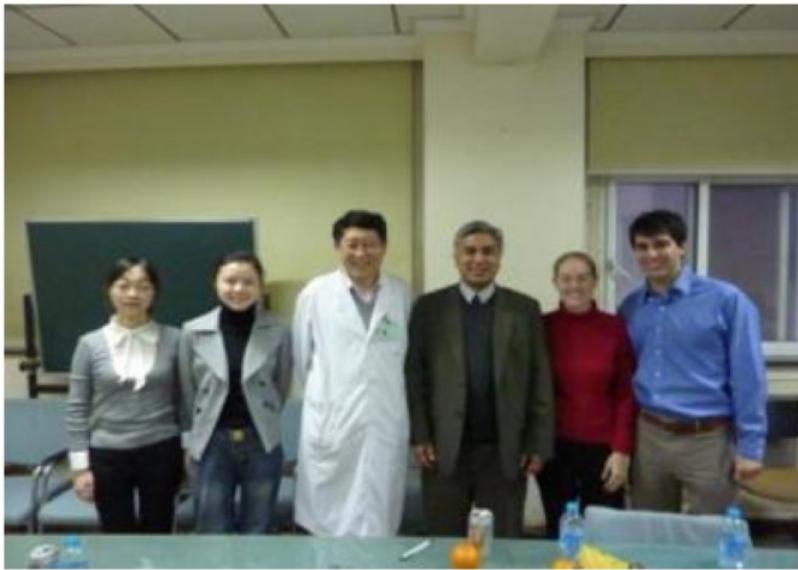
MD

SD/CIS

1. Dawsey SM, Lewin KJ, Liu FS, Wang GQ, Shen Q. Esophageal morphology from Linxian, China. Squamous histologic findings in 754 patients. *Cancer*. 1994 15;73(8):2027-37.
2. Dawsey SM, Wang GQ, Weinstein WM, Lewin KJ, Liu FS, Wiggett S, Nieberg RK, Li JY, Taylor PR. Squamous dysplasia and early esophageal cancer in the Linxian region of China: distinctive endoscopic lesions. *Gastroenterology*. 1993 ;105(5):1333-40.
3. Wang GQ1, Abnet CC, Shen Q, Lewin KJ, Sun XD, Roth MJ, Qiao YL, Mark SD, Dong ZW, Taylor PR, Dawsey SM. *Gut*.2005; 54(2):187.

1.3 Educational training programs

- 1. Cancer Prevention Academic Course by DCPC/NCI since 1986**
- 2. NIH Fogarty International Clinical Research Scholars & Fellow Program (FICRS)**
- 3. NIH-Fulbright Public Health Program in CICAMS/PUMC**
- 4. Fogarty Global Health Fellows 2013-2014
UNC-CH/Hopkins/Morehouse/Tulane
(Qiao/Smith/Zhao)**



Myat Htoo Razak visited the Fogarty site, Beijing, 2010)



Alumni of National Institutes of Health (Beijing, Oct. 14, 2010)



Fogarty scholars with **Dr Roger Glass**, Beijing, 2012



Fogarty scholars with **Ms Kathleen Sebelius**, Secretary of HHS , U.S.



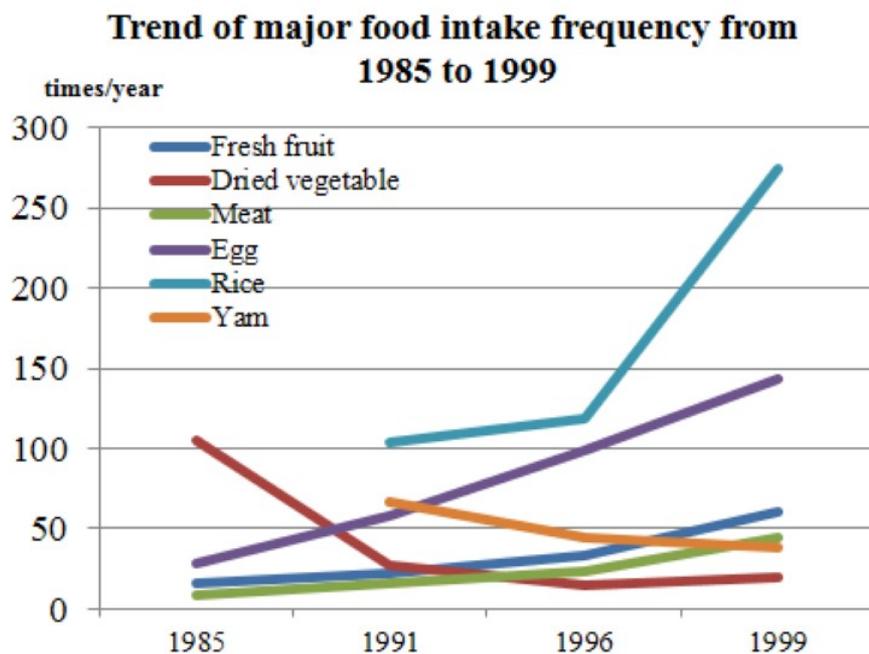
**Fogarty-Fulbright Scholars/mentor with Dr. Harold Varmus, Nobel Laurel and Director of NCI/NIH, USA in Cancer Inst. Chinese Academy of Medical Sciences
Beijing, China, March 17, 2013**

2. Impact of NCI-CICAMS collaborations - NIT

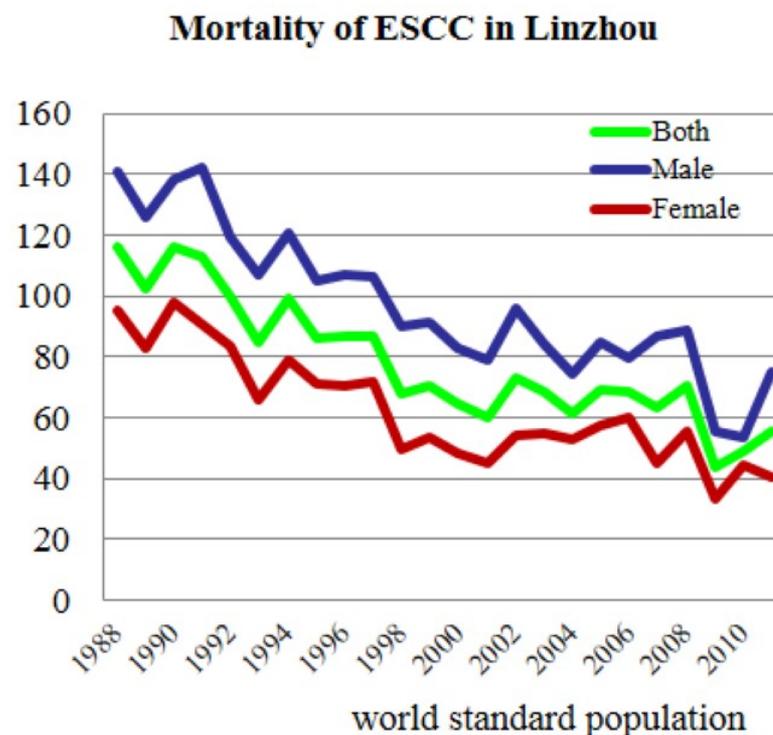
For the people of Linxian

- Provide evidence for considering a public health action plan
- Reduce mortality of common cancers and elderly diseases

Nutrition changes



Rates changes



2.2 Impact of NCI-CICAMS collaborations - Screening

Taihang Mountain Anti-cancer Campaign: Demonstration center

Population based cancer prevention program

Multi-center endoscopic screening evaluation study in high risk population

2005: 2 high risk areas (Demonstration)

2007-2012: 7-121 Rural high risk areas in 27 provinces

Colorectal cancer: 15 sites in 11 provinces

Liver cancer: 11 sites in 4 provinces

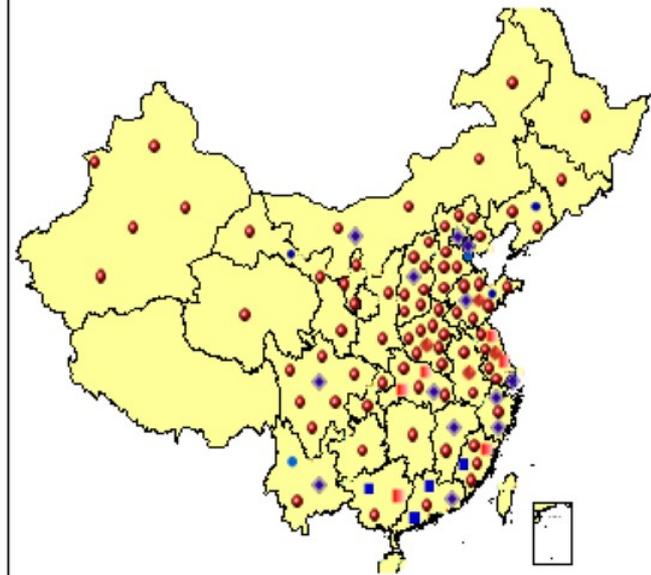
Nasopharyngeal cancer: 6 sites in 3 provinces

Lung cancer: 3 sites in 2 provinces

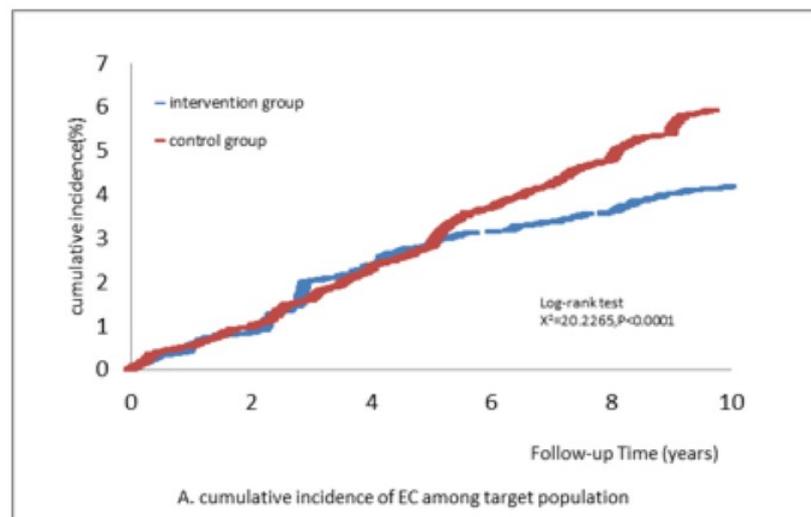
Huai River Region: 26 sites in 4 provinces

Cervical cancer: 10M/year in 1000+ sites

Breast cancer; 1.2M/year in 220+ sites

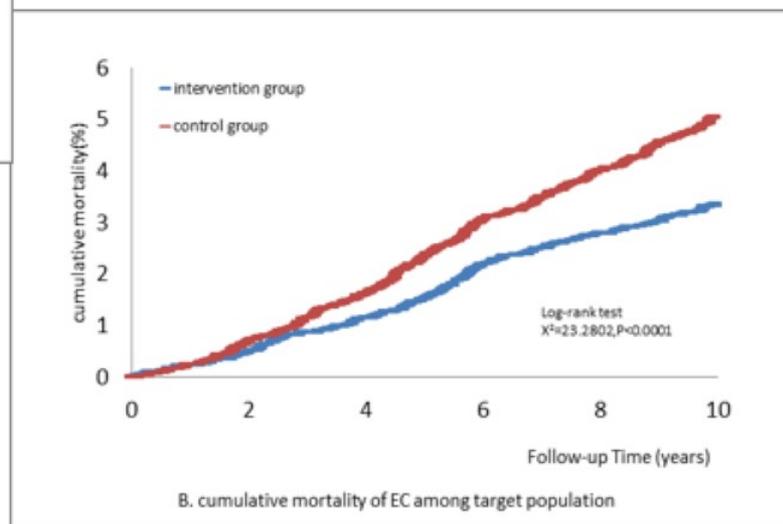


Long-Term Follow-Up of a Community Assignment, One-Time Endoscopic Screening Study of Esophageal Cancer in China



Cumulative **Incidence of EC**
among the target population
4.17% vs 5.92%. reduced **29.47%**

Cumulative **Mortality of EC**
among the target population
3.35% vs 5.05% reduced **33.56%**



Wei WQ, Chen ZF, He YT, Feng H, Hou J, Lin DM, Li XQ, Guo CL, Li SS, Wang GQ, Dong ZW, Abnet CC, Qiao YL. Long-Term Follow-Up of a Community Assignment, One-Time Endoscopic Screening Study of Esophageal Cancer in China. J Clin Oncol. 2015 May 4. pii: JCO.2014.58.0423.

2.3 Impact of NCI-CICAMS collaborations - Ethics

- **IRBs modeled on NCI projects in 1984**
 - Members
 - Initial review
 - Continuing annual review
 - Fixed date vs. by request
- **Single project assurance (SPA)**
- **Multiple project assurance (MPA)**
- **Routine for all human related studies**

2.4. Health Policy and Regulatory (CGH)

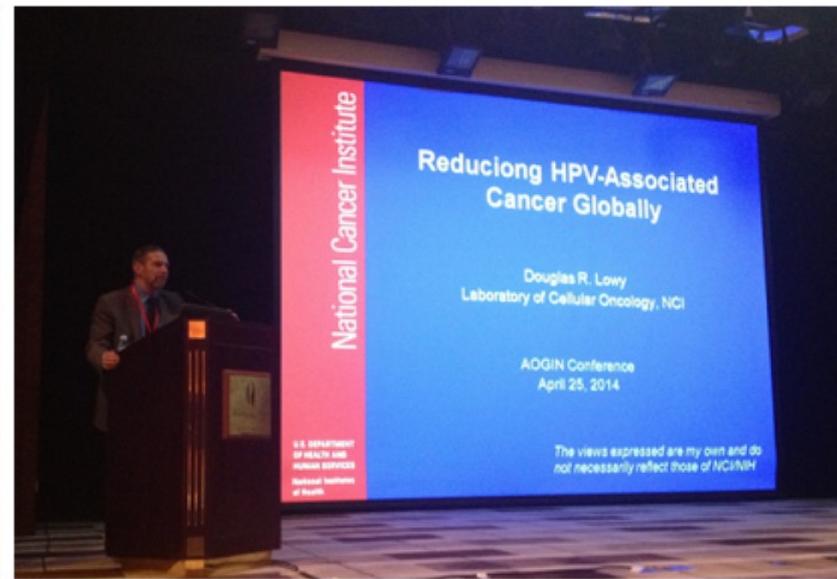
Roundtable Discussions for

- ➡ HPV vaccine implementation in China
- ➡ Comprehensive prevention of cervical cancer in China



The Asia Oceania Research Organization on Genital Infections and Neoplasia (AOGIN) Biennial Conference April 25-27, 2015 Beijing

- ➡ Dr Lowy's Keynote Speech "Reducing HPV-Associated Cancer Globally"
- ➡ CGH Session- "Evaluation and Follow up in Cervical Cancer Screening Programs, No Woman Left Behind" by Dr. Ted Trimble
- ➡ DCP Session- "Cancer Immunoprevention: Current Status and Future Directions for Cervical Cancer Prevention" by Asad Umar



Promote governmental collaboration to prevent cervical cancer in Asia (CGH)

- ➡ The 1st Senior Officials' Meeting (SOM1) & Related Meetings
- ➡ APEC delegations from US and China in Ningbo Feb, 2014



*Regional Workshop on Enabling Sustainable Economic Advancement
for Women through Cervical Cancer Prevention and Control*



Asia-Pacific
Economic Cooperation

APEC CHINA 2014

August 16, BEIJING



NATIONAL
CANCER
INSTITUTE



APEC
CHINA 2014

78 delegates from the governments, academic institutions and international organizations of 11 economics exchanged opinions in terms of research, clinical treatment and health policy, also discussed and identified the gaps to building and strengthening the capacity for cervical cancer prevention and control.

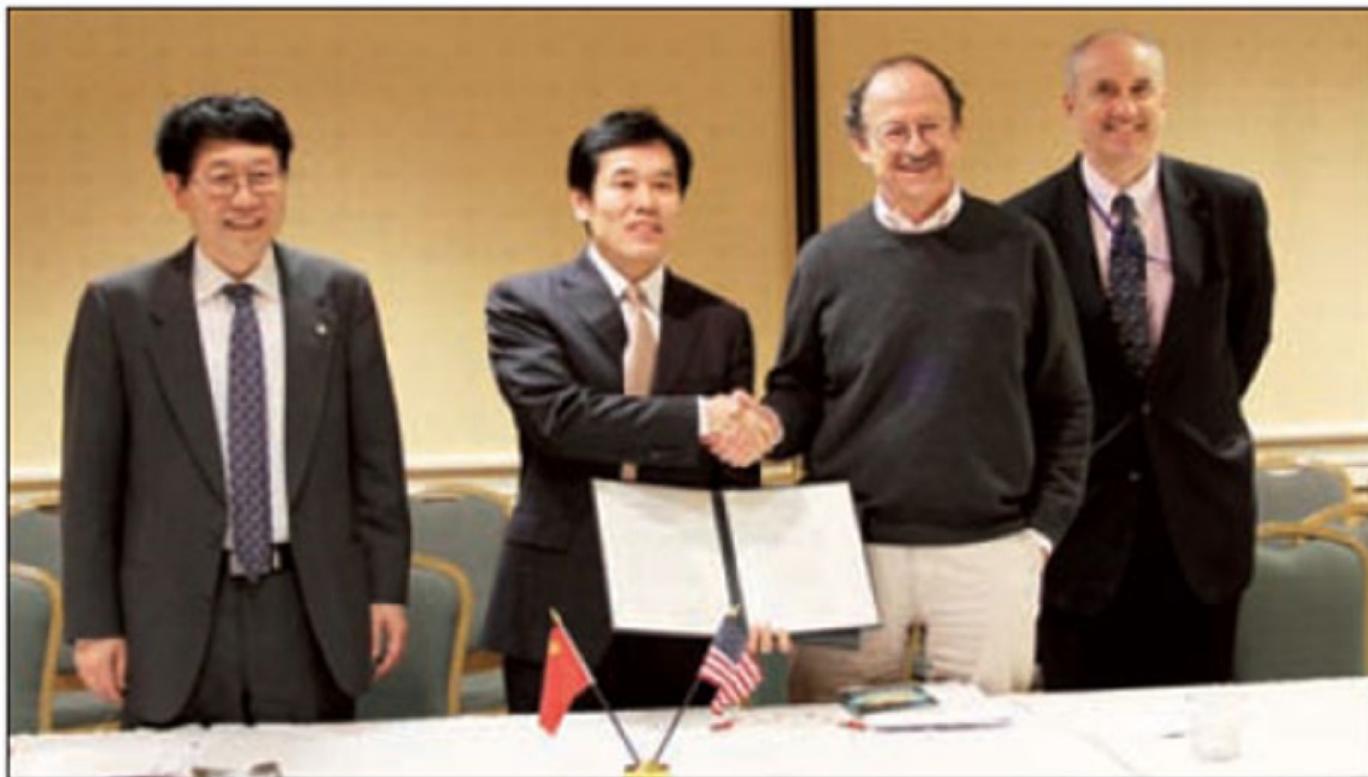


**First Workshop on Using Cancer Registry Data to Inform Cancer
Research and Cancer Prevention and Control Policy**
**Chinese National Cancer Center, Chinese CDC, Shanghai CDC,
CGH/NCI, WHO/IARC**



3. Future collaboration

US, China combine efforts to study cancer
By Wang Chao in Washington (China Daily)



SUN CHENBEI / CHINA DAILY

He Jie (second left), president of CICAMS, shakes hands with Harold Varmus, director of NCI at the signing ceremony, while Qiao Youlin (first left) from CICAMS and Ted Trimble from NCI look on.

3. Future collaborations - 2

- Follow-up Study of Nutrition Intervention Trials in Linxian (30-year data analysis)
- Serum Nutritional Biomarkers & Common Cancers
- Esophageal Cancer Family Study, Linxian, China
- Prospective Evaluation Study of Upper GI Cancer Screening based on the demonstration centers
- Biological markers of early detection for ESCC

3. Future collaborations - 3

- **National Cervical Cancer Prevention Plan and Strategies in China**
 - **Dr. Fang-Hui Zhao under the guidance of Dr. Lowy**
- **The Need for National Commitments to Cancer Research to Guide Public Health Investment and Practice (collaborating with CGH)**
- **Build and strengthen the networks of cervical cancer prevention in Asian Pacific Areas through APEC and AOGIN (collaborating with CGH)**
- **The NCI Summer Curriculum in Cancer Prevention in China (collaborating with CGH and DCP)**
- **Collaborations with National Cancer Registry Center**