National Cancer Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

CENTER FOR GLOBAL HEALTH

Overview: NCI Center for Global Health

Edward L. Trimble, MD, MPH
Director, Center for Global Health
National Cancer Institute, NIH, US DHHS

November 2017

NCAB

Harold Varmus, MD

- Nobel Prize for Medicine, 1989
- Director, US NIH, 1993-1999
- Director, Memorial Sloan-Kettering Cancer Center, 2000-2010
- Director, US NCI, 2010-2015

US NCI Priorities in Global Health

- Strengthening global cancer research
- Building a global cancer research community
- Translating research results into practice

- Based on cancer research stakeholders meeting, 2012

US Partners: I

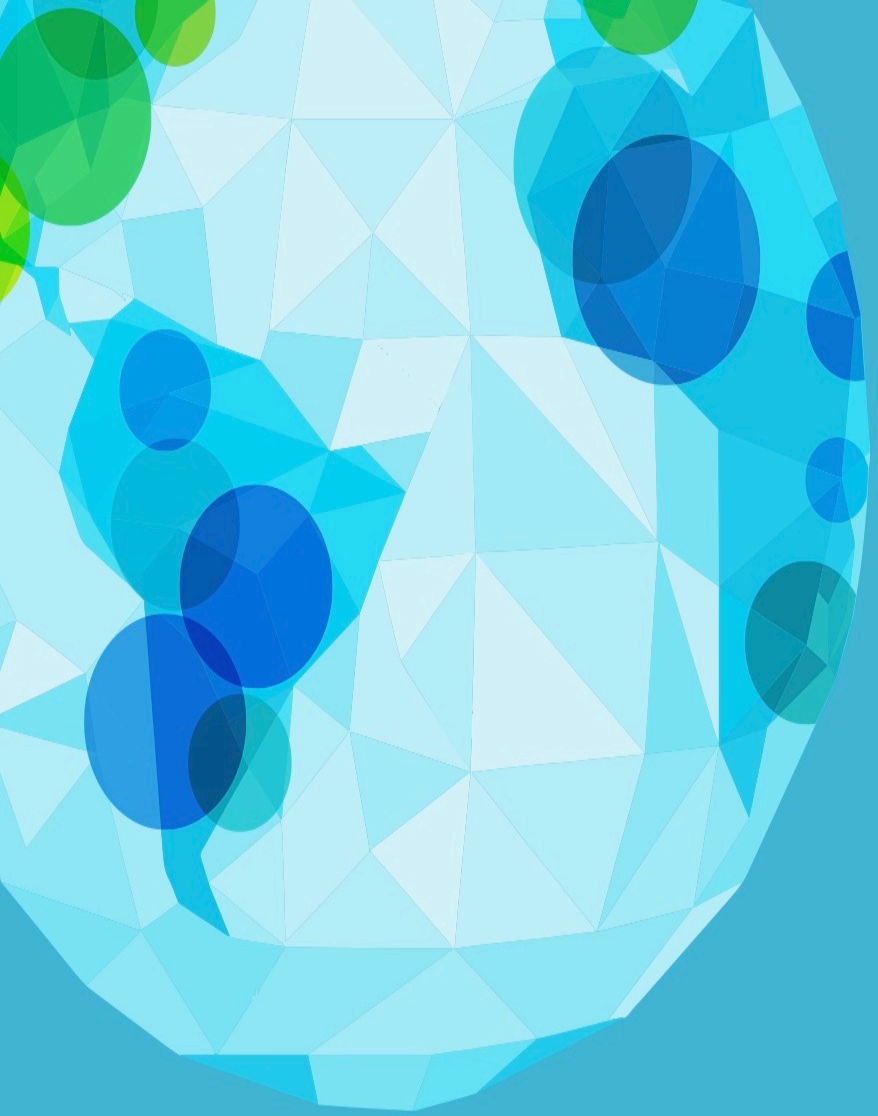
- NCI Divisions, Offices, & Centers
- NCI-designated Cancer Centers
- Fogarty International Center & other NIH Institutes & Centers
- CDC
- USAID, PEPFAR, Department of State

Partners: II

- Professional societies
- Cancer advocacy groups
- WHO, IARC, WHO Regional & Country Offices
- International Atomic Energy Agency
- International Union for Cancer Control
- Global & national cancer research funders
- National & state governments

Agenda

- NCI Leadership
- Global pediatric cancer
- Working with NCI-designated Cancer Centers
- Affordable Cancer Technology
- Improving access to cancer drugs in Africa
- New business

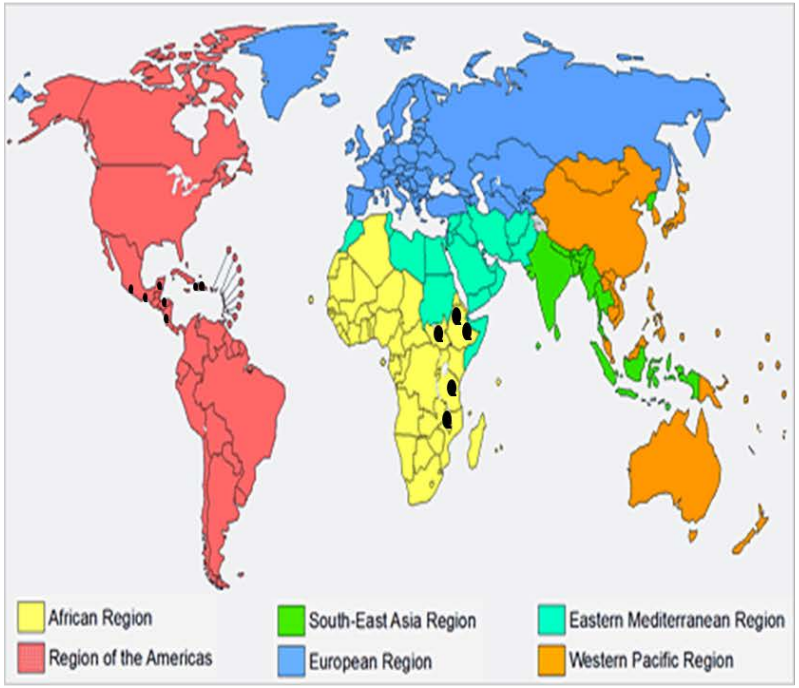


Burkitt Lymphoma Research Network

Burkitt Lymphoma Research Network Strategy (SPL: January, 2015)

- Issue a cooperative agreement to fund a clinical coordinating center for the BL research network
- **Step 1: Build and strengthen BL research capabilities in Low- and Middle-income Countries (LMICs)**
  - Low Investment - High-impact pilot research projects via P30 Administrative Supplements

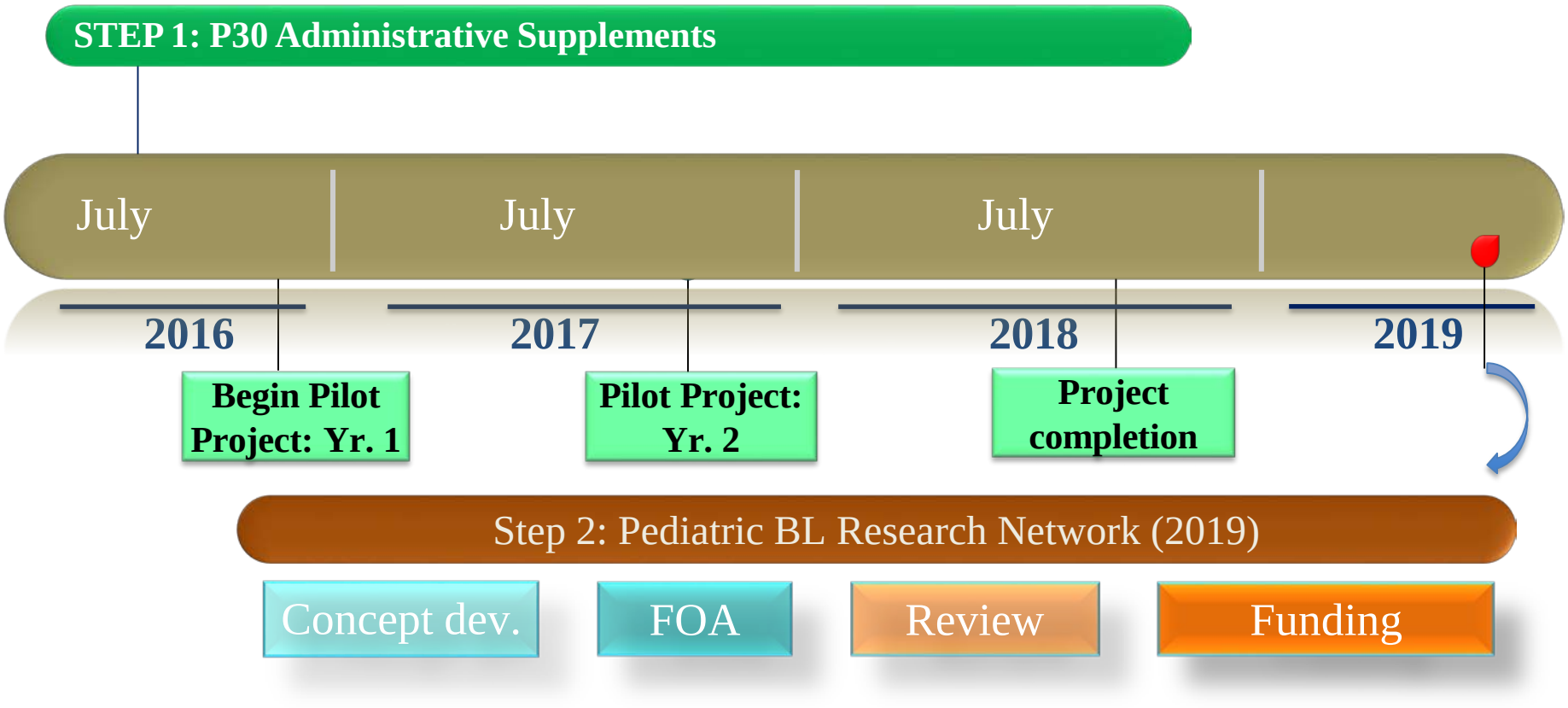
Pediatric Burkitt Lymphoma Research Sites



Grant Number	Cancer Center	LMIC Institution
CA016086-40S4	UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL	Kamuzu Central Hospital, Lilongwe, Malawi
CA125123-10S5	BAYLOR COLLEGE OF MEDICINE	Uganda Cancer Institute, Kampala, Uganda
CA082709-17S3	INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS	MOI Teaching and Referral Hospital, Eldoret, Kenya
CA014236-42S1	DUKE UNIVERSITY	Bugando Medical Centre, Mwanza, Tanzania
CA082709-17S4	INDIANA UNIV-PURDUE UNIV AT INDIANAPOLIS	Jaramogi Oginga Odinga Teaching and Referral Hospital, Kisumu, Kenya

Africa: Malawi; Uganda; Tanzania; Kenya (Eldoret and Kisumu)
Central America and Caribbean: Costa Rica; Dominican Republic; El Salvador; Guatemala; Haiti; Honduras; Nicaragua

Pediatric BL Research Network



Background: NCI-Designated Cancer Centers

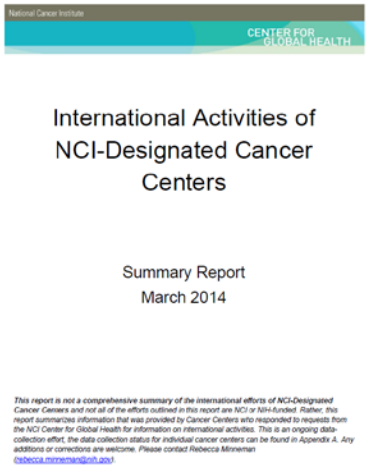
- **CGH aimed to leverage NCI-Designated Cancer Centers to support research in LMICs**
- 69 Centers in 35 US states and DC
- Backbone of NCI's programs for studying and controlling cancer
  - Investigators at Cancer Centers **receive ¾ of NCI awarded investigator-initiated grants**
  - NCI grants to Cancer Centers support **shared research resources**, provide **developmental funds** to advance scientific goals, and **foster interdisciplinary initiatives**
  - Centers are recognized for scientific leadership, research resources, and the **depth and breadth of research:** hundreds of ongoing research studies across the translational continuum
- **Challenge:**
  - When CGH was created, there was no extant database of Cancer Centers' international activities (NCI funded or not).
  - How best to engage Cancer Centers, given limited knowledge of their existing international activities?

Background: CGH Engagement with the Cancer Centers

CGH engaged in two activities to gather information….

(1) **Data calls to all NCI-Designated Cancer Centers, 2012, 2013, 2014**

- Answered questions such as:
  - Which countries are NCI Designated Cancer Centers working in?
  - Who are their partner institutions in LMICs?
  - What are their focus areas? (e.g., cancer sites, where on the cancer continuum – Dx, Tx, palliative care, etc.)
  - What types of activities are they engaged in? (e.g., research, training, infrastructure development)
- High level of reported activities:
  - e.g., 2014: 56 of 68 Cancer Centers reported international activities
- Data used to plan for future CGH engagement with Cancer Centers, including two funding opportunities (next slide)



Background: CGH Engagement with the Cancer Centers

(2) Two funding opportunities for scientists at Cancer Centers to partner with scientists at LMIC institutions to advance cancer research in LMICs

- 2014 -- One-year contracts up to $200,000

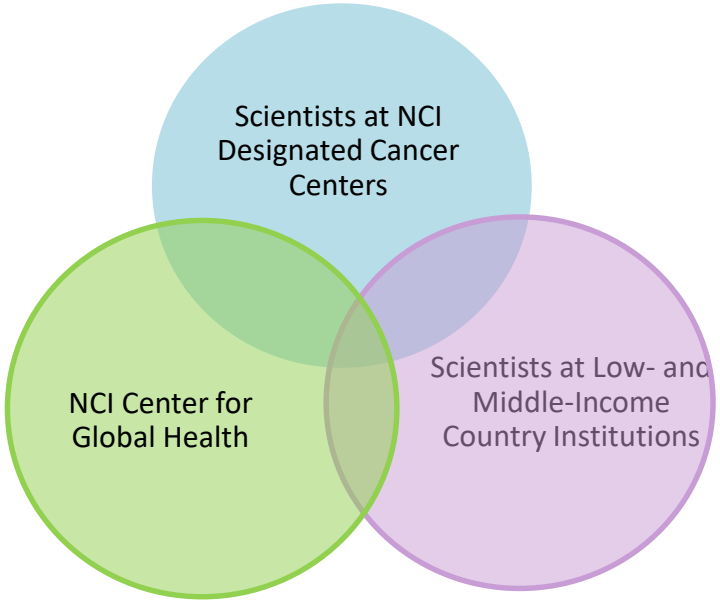
  Broad scope: cancer research, research training, and/or research infrastructure development in LMICs

  - Awarded to 15 of 43 proposals
  - All final reports received by Jan 1 2016

- 2015 -- Two-year administrative grant supplements up to $260,000

  Narrower scope: research focused on cancer prevention and control in LMICs

  - Awarded to 10 of 39 applications
  - All final reports submitted by Jan 1 2018
  - Analysis forthcoming

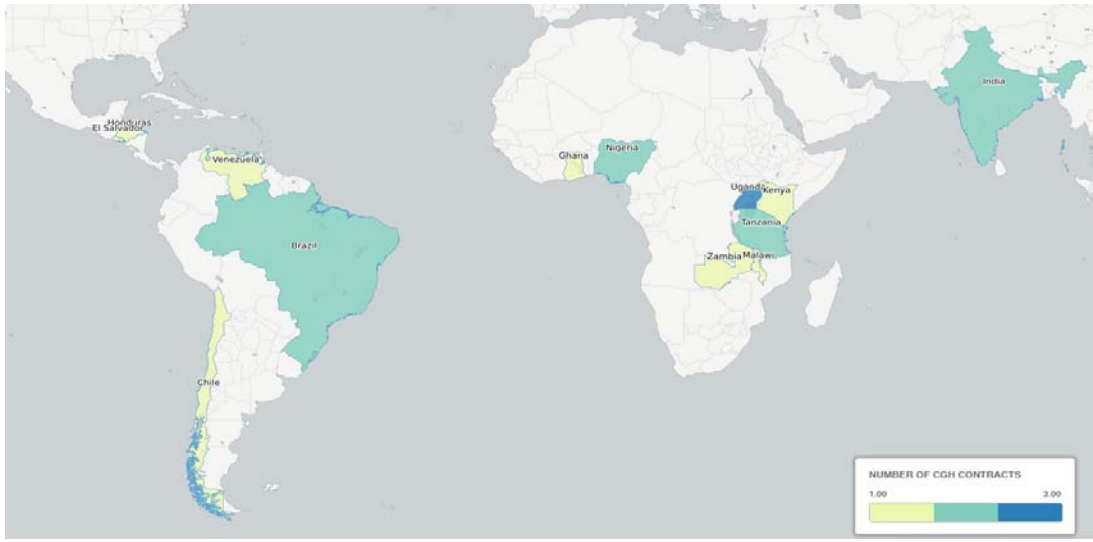


Geographic distribution of awarded activities

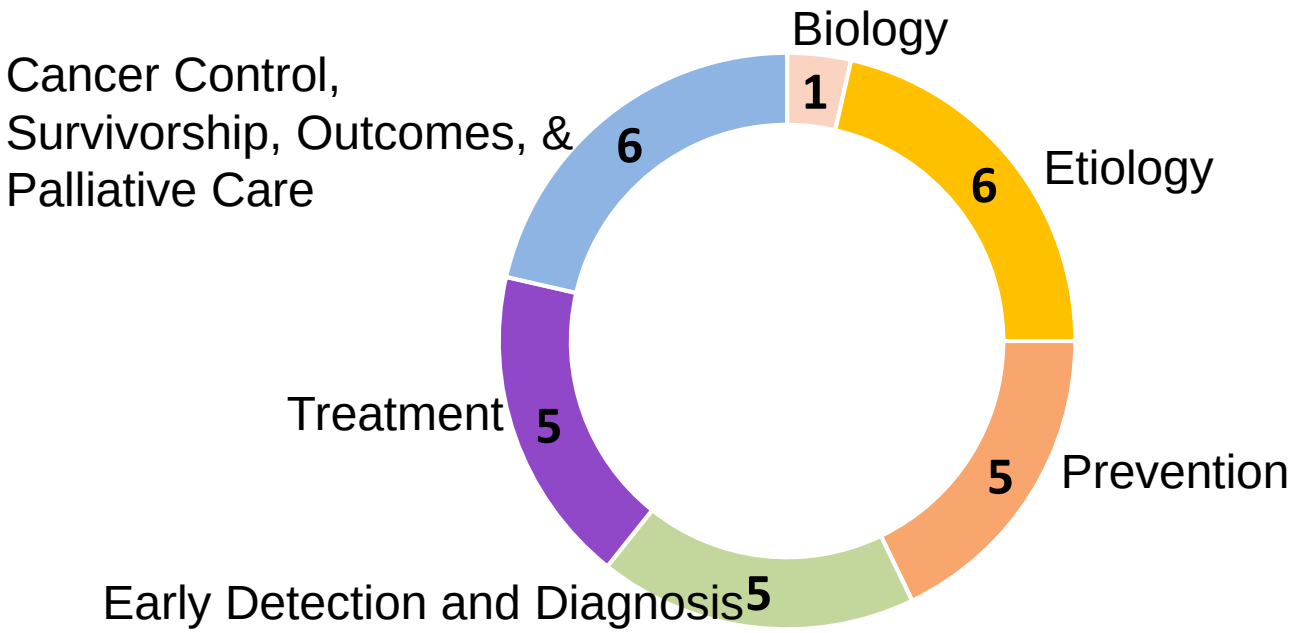
Contracts:	15
Partner institutions:	19
Countries:	13
Contracts in Africa:	**9, in 7 countries**
Contracts elsewhere:	6, spread over 3 regions

Concentrations of activity:

- Uganda (3 contracts)
- Brazil, India, Nigeria, and Tanzania (2 contracts, each; total of 8)



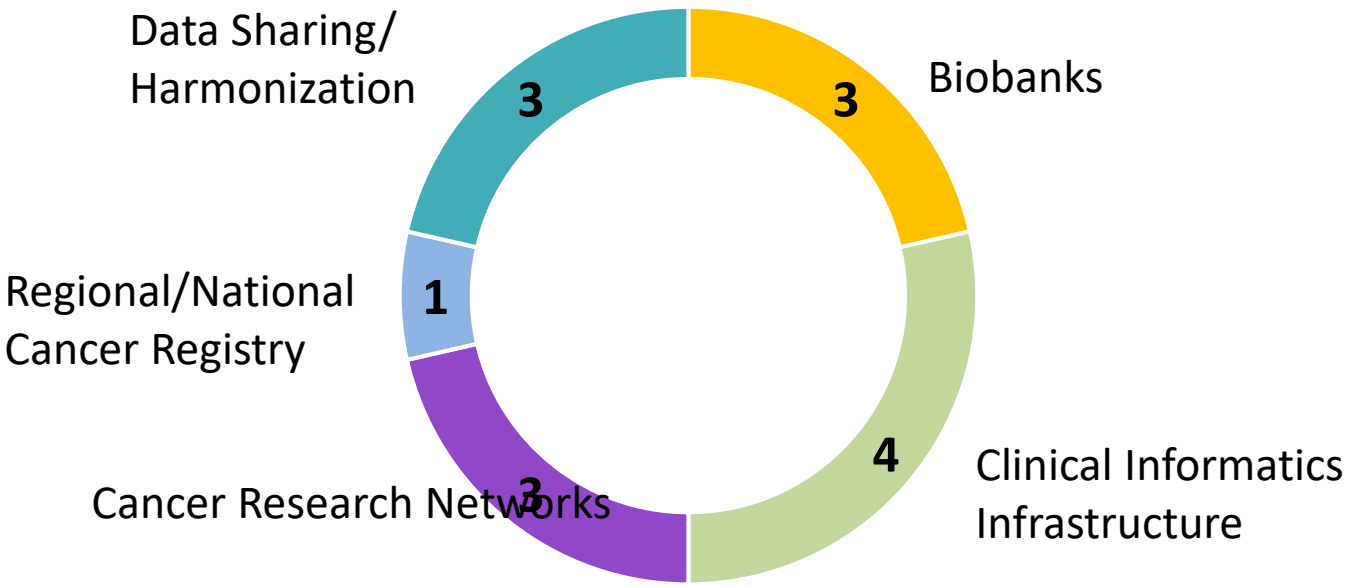
Areas of Scientific Interest: CSO Codes



- 15 projects addressed the full range of all six CSO codes
- Emphasis equally spread across all codes except biology
- **Shows a focus on applied research that addressed the needs in these settings**

NOTE: Does not sum to 15, as many projects addressed multiple areas of scientific interest.

Investments in Research Infrastructure



- 7 of 15 projects included 1ary or 2ary aim to develop sustainable infrastructure for cancer research in LMICs.
- Reflected 21st century approaches, e.g., biobanking, medical informatics that include images, cloud-based data sharing

NOTE: Does not sum to 7, as some of the projects created 2+ types of research infrastructure.

Learn more about cancer research partnerships between Cancer Centers and LMIC institutions

- Did funded partnerships predate this funding opportunity?
- How did this funding opportunity contribute to these partnerships?

Partnerships

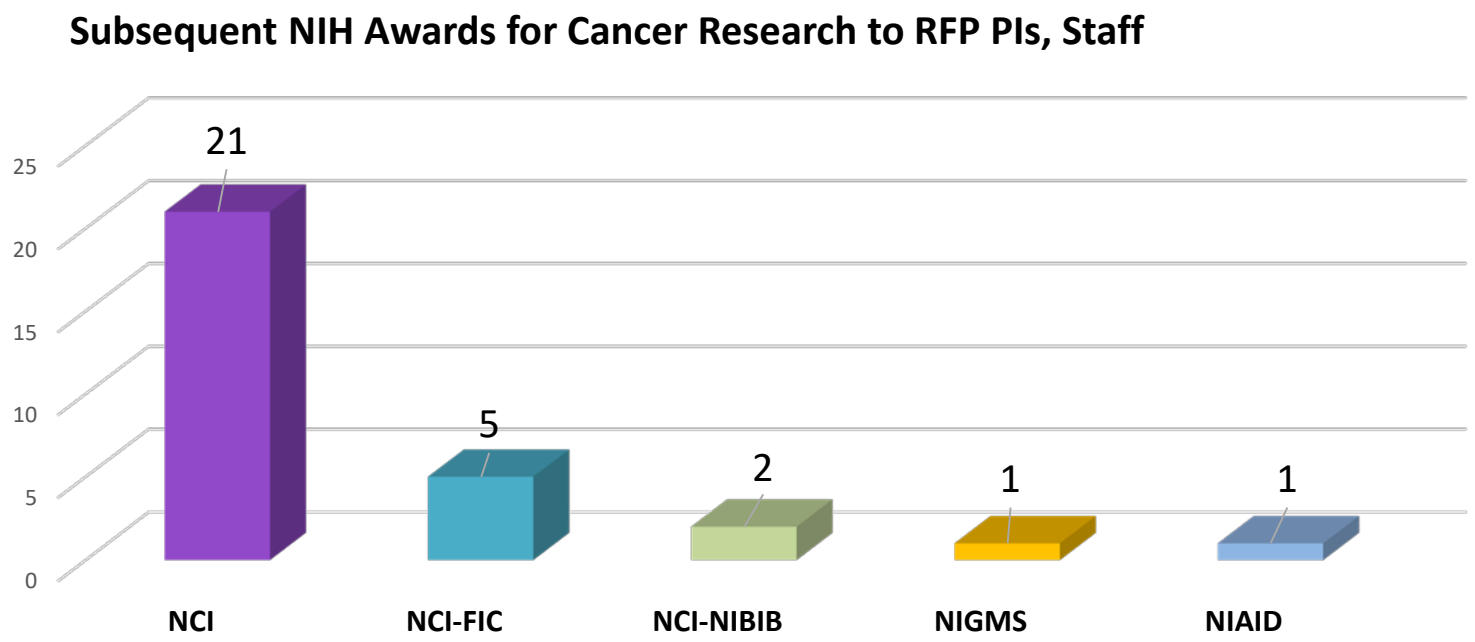
- 14 of 15 contracts built on **preexisting partnerships** between the Cancer Center and 1 or more partnering LMIC institutions
  - 2 to 24 years duration
  - Only 1 partnership appeared to be entirely new, and encountered unanticipated challenges related to lengthy IRB review at LMIC partner institution
- 6 used contract as an opportunity to **add additional LMIC institutions** to the partnership
  - Forming sub-national, national, and regional partnerships
  - Facilitating South-to-South capacity building relationships

- Cancer Centers are **investing in** preexisting partnerships
- They are also **leveraging** preexisting partnerships, making for efficient science
- They are investing in efforts to **expand partnerships** in LMICs

Garner insights into **how funding opportunities like this one contribute to supporting continuing programs of cancer research** in LMICs

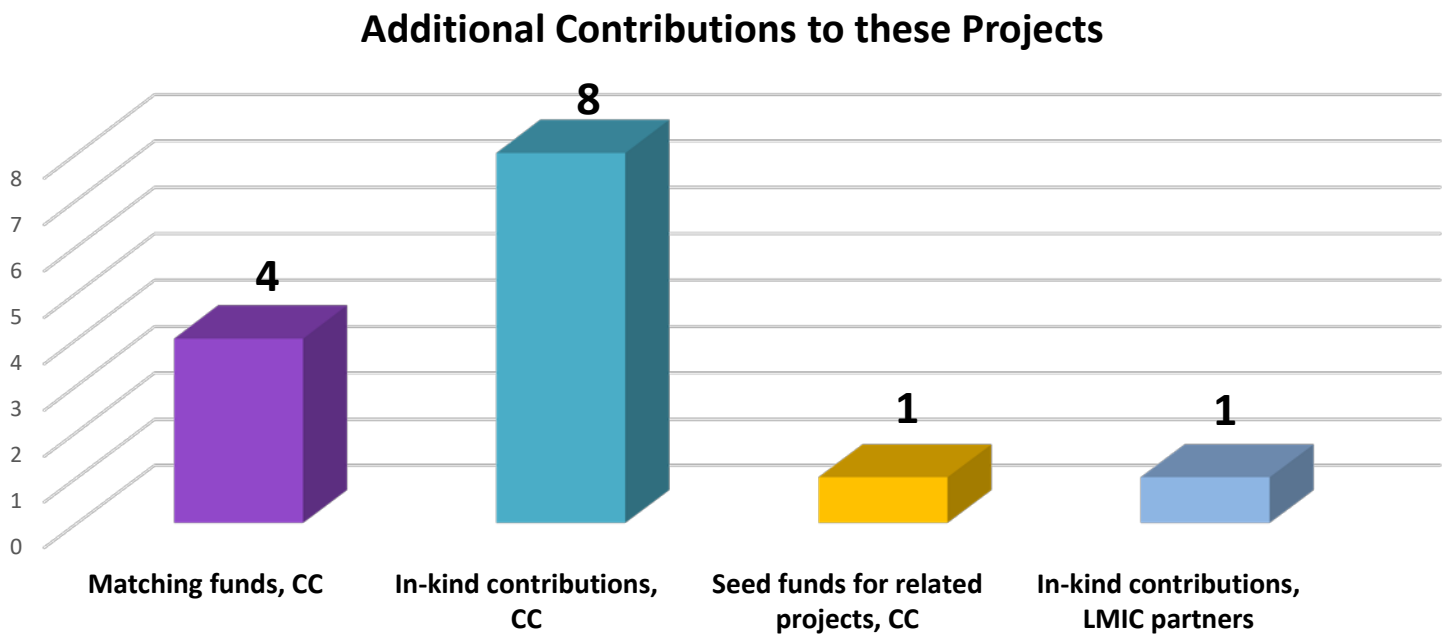
- Subsequent related awards
- Matching contributions by Cancer Centers in LMIC settings

Subsequent Related Awards



- 32 subsequent NIH awards to 95 investigators and staff listed on the 15 contract proposals
- 30 awards were cancer-related; 28 were funded or co-funded by NCI
- **Contract was one "stepping stone" in ongoing programs of cancer research; suggests this research was relevant to LMICs**

Additional Contributions



- 11 of 15 contracts reported additional investments by the Cancer Center
- **Demonstrated commitment to LMIC research and partnerships**

Four key take-aways for planning future engagement with grantees

1) **Supported activities both addressed needs in LMIC settings and capitalized on LMIC settings to advance cancer science more broadly: notably, infection-related cancers (8 projects), genomics (4 projects), and applied research (e.g., Dx, Tx)**
    - Highlights potential areas of focus for future initiatives

2) **7 of 15 projects included a primary or secondary aim to develop sustainable infrastructure for cancer research in LMICs**
    - Also a potential areas of focus for future initiatives
    - NOTE: Subsequent CGH RCREs award (2016) focuses on research resources (Regional Centers of Research Excellence in Non-Communicable Diseases in Low and Middle Income Countries)

Four key take-aways for planning future engagement with grantees

3) **Preexisting partnerships were valuable and valued**

- Supported efficient research, leveraged to expand networks, garnered matching/in-kind contributions
- Future initiatives may wish to build on existing partnerships in LMICs, and explicitly encourage expansions as seen in this cohort

4) **These small awards were a "stepping stone" in a history of funding**

- Leveraged for matching/in-kind contributions
- Connected to 30 subsequent cancer related awards in only 3 years
- Small awards may be effective contributors to ongoing programs of research, stimulating additional investments

NCDs Have Common Risk Factors

- Tobacco use
- Physical inactivity
- Unhealthy diet
- Harmful use of alcohol
- Environmental factors
  - Outdoor air pollution
  - Indoor air pollution

Proposal for Regional Centers of Excellence in Cancer & NCD Research

- Cancer & non-communicable diseases in low- and middle-income countries
  - Broad definition of NCDs, includes mental health, trauma, surgery, hematology, palliative care, etc
- Planning grants (P20), $200,000 per year for 2 years
- Consortia of HIC and LMIC institutions working in selected region or country

Purpose and Strategy of the P20 NCD Centers of Research Excellence (P20), RFA CA15-007

Purpose:

To support the planning and design of cancer & NCD-focused, research centers of excellence in low- and middle income countries

Strategy:

- Develop a hypothesis-driven research plan that specifies the short-, mid- and long-term outcomes for the two NCD research programs;
- Create a well-justified plan for consolidating existing or opening new shared core facilities;
- Complete a local needs assessment; and
- Incorporate concrete metrics for monitoring and evaluating the quality, value, and scientific impact of the RCRE on the region

RCRE in Cancer and Other NCDs Disease Epidemiology and Prevention in Vietnam

P20 CA210300

co-PI: Dr. Xiao-Ou Shu Vanderbilt University
co-PI: Dr. Thuan Van Tran National Inst. for Cancer Control Vietnam

Description of Project:

To build a RCRE in Vietnam to establish **a large population-based cohort study to examine the influence of westernization on NCDs in Vietnam**

Anticipated Outcomes from the Pilot Studies:

- Case-control study for **breast cancer**
- Cross-sectional community-based survey of **type 2 diabetes**

Shared Resources:

- Survey Research Support Core
- Biospecimen Processing and Biorepository Core
- Bioinformatics and Informatics Core

RCRE in South Africa and Botswana

P20 CA210283

co-PI: Dr. Neo Tapela — Botswana Harvard AIDS Institute
co-PI: Dr. Bruce Chabner — Massachusetts General Hospital
co-PI: Dr. Shahin Lockman — Harvard Medical School
co-PI: Dr. Doreen Ramogola-Masire — Botswana UPenn Partnership

Description of Project:

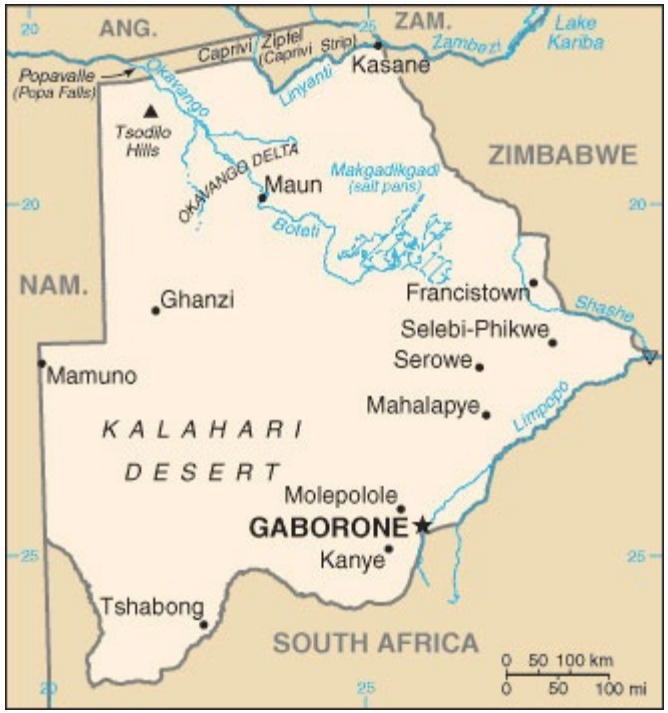
To strengthen data for **breast cancer, hypertension, and road-traffic accident trauma research** in Botswana and South Africa

Anticipated Outcomes from the Pilot Studies:

- To develop eHIS in South Africa to generate quality data elements for breast cancer studies
- To expand the Integrated Patient Management System in Botswana to include HTN and trauma

Shared Resources:

- Data acquisition
- Data aggregation and management
- Biostatistics



RCRE in Malawi

P20 CA210285

co-PI: Dr. Satish Gopal — University of North Carolina Chapel Hill

co-PI: Dr. Dirk Dittmer — University of North Carolina Chapel Hill

co-PI: Dr. Mwapatsa Mipando — University of Malawi College of Medicine

co-PI: Dr. Nyengo Mkandawire — University of Malawi College of Medicine

Description of Project:

To build a RCRE in Malawi that will serve as regional research resource for **cancer pathology and trauma surgery training**

Anticipated Outcomes from the Pilot Studies:

To identify a molecular signature carcinogen-associated esophageal squamous cell carcinoma

Shared Resources:

- Clinical
- Laboratory
- Epidemiology

Mesoamerican Center for Population Health Research on NCDs
Mexico, Guatemala, Costa Rico, and Colombia

P20 CA210286

co-PI: Dr. Martin Lajous — Instituto Nacional de Salud Publica

co-PI: Dr. Ruy Lopez-Ridaura — Instituto Nacional de Salud Publica

Description of Project:

To pool existing expertise, resources and infrastructure to build sustainable **cancer and diabetes research** programs

Anticipated Outcomes from the Pilot Studies:

To analyze prospective observational data from the MTC to provide evidence about the social and biological risk factors for NCDs

Shared Resources:

- Study Design, Analysis, and Dissemination Unit
- Human Subjects' Research Unit
- Funding Opportunity Monitoring and Gra

Bangladesh Center for Research Excellence in NCDs

P20 CA210305

co-PI: Dr. Habibul Ahsan University of Chicago

co-PI: Dr. Syed Shariful Islam Bangabandu Sheikh Mujib Medical University

Description of Project:

To investigate the determinants of **women's cancers and CVD** to lead to better informed policies and care in Bangladesh

Anticipated Outcomes from the Pilot Studies:

To create a pathology-based cancer registry to study the distribution of breast, uterine, & cervical cancers

To evaluate how the gut microbiome contributes to subclinical markers of CVD

Shared Resources:

- Data Management, Statistics and Informatics Core
- Biomarker Core
- Population Survey and Data Collection Core
- Clinical and Diagnostics Core

RCRE in India

P20 CA210298

co-PI: Michael Goodman — Emory University

co-PI: Dorairaj Prabhakaran — RTI Global India Private Limited

Description of the Project:

To develop a unified, country-wide, population-and clinic-based RCRE to prevent and control **breast cancer, oral cancer, and diabetes** in India

Proposed Pilot Studies:

To develop a standard methodology to link rich population-based cohort data with cancer morbidity data fromregistries to scale-up investigation

Shared Resources:

- Biorepository/laboratory
- Data management
- Field data collection

Photo of Delhi, India
Photo credit:
https://www.duolingo.com/comment/6352570

Building Sustainable and Innovative Research in Cancer and Cardiovascular Disease

P20 CA217231

co-PI: Dr. Adolfo Rubinstein IECS – Instituto de Efectividad Clinica Y Sanitaria
co-PI: Dr. Juan Jaime Miranda UPCH – Universidad Peruana Cayetano Heredia
co-PI: Dr. Deborah Schrag DFCI – Dana-Farber Cancer Institute

Description of Project:

- To establish a large population-based cancer and CVD cohort to identify common risk factors, potential treatment gaps, and health disparities in the Southern Cone of South America

Strengths of the Application:

- Innovative, impactful, and collaborative pilot project to geo-map gallbladder and stomach cancer in South America
- Highly integrative with the existing initiatives in the region
- Abundant support from the health ministers of Argentina and Peru
- Clear milestones and realistic goals

Planning for a Sustainable and Innovative Robust RCRE in the Caribbean

P20 CA210294

co-PI: Dr. Camille Ragin — Institute for Cancer Research

co-PI: Dr. J. Robert Beck — Research Institute of Fox Chase Cancer Center

co-PI: Dr. Marshall Tulloch-Reid — University of the West Indies

co-PI: Dr. Kenneth James — University of the West Indies

Description of Project:

- To conduct foundational activities that will lead to a RCRE focused on prostate cancer and CVD research

Strengths of the Application:

- Clear evaluation framework
- Program builds on existing collaborations and NIH-funded initiatives
- Leadership team is balanced with appropriate expertise including laboratory, population, clinical, and decision sciences

Building Research Capacity to Address the Challenge of NCDs and Injuries in Rwanda: the GUKORANA Research Center

P20 CA210284

co-PI: Dr. Jean Claud Byiringiro University of Rwanda

co-PI: Dr. Philip Castle Albert Einstein College of Medicine

Description of Project:

To build a RCRE in Rwanda that focuses on gynecological cancers and injury

Strengths of the Application:

- Builds upon existing EMR and cancer registry data
- Builds on existing HIV related services and PEPFAR collaborations in the region
- Environment is excellent; agreements are in place to allow for larger scale studies in the future

African Center for the Advancement of Research Excellence (Africare)

P20 CA210677

co-PI: Dr. Thomas Campbell University of Colorado, Denver
co-PI: Dr. Margaret Borok University of Zimbabwe
co-PI: Dr. James Hamim University of Zimbabwe
co-PI: Dr. Edward Havranek University of Colorado, Denver

Description of Project:

To improve the prevention, recognition, and outcomes of **CVD** and breast **cancer**

Strengths of the Application:

- Institutional facilities and resources are well leveraged to accomplish research activities
- Evaluation metrics are comprehensive, reasonable, and measurable

Stanford – Colombia Collaboratory on Chronic Disease Prevention

P20 CA217199

co-PI: Dr. Abby King Stanford University
co-PI: Dr. Olga Sarmiento Universidad de los Andes

Description of Project:

To facilitate physical activity based interventions to prevent breast cancer, diabetes, CVD, and depression

Strengths of the Application:

- Established, accomplished investigators with diverse and complementary expertise
- Application builds on existing national multi-sectorial programs

Planning for the Southern Africa (Lesotho, South Africa, Swaziland, Zambia, and Zimbabwe) RCRE for NCDs

P20 CA217242

co-PI: Dr. Wafaa El-Sadr Columbia University Health Sciences
co-PI: Dr. Alfred Neugut Columbia University Health Sciences
co-PI: Dr. Shane Norris Wits Health Consortium

Description of Project:

To improve access to cervical cancer and HTN screening, diagnosis, prevention, and treatment

Strengths of the Application:

- Complements and builds on other research programs in the region
- Outstanding scientific expertise of the principal investigators
- Leveraging and sharing of existing research resources

National Cancer Institute

CENTER FOR GLOBAL HEALTH

Affordable Cancer Technologies (NCI ACTs) Initiative

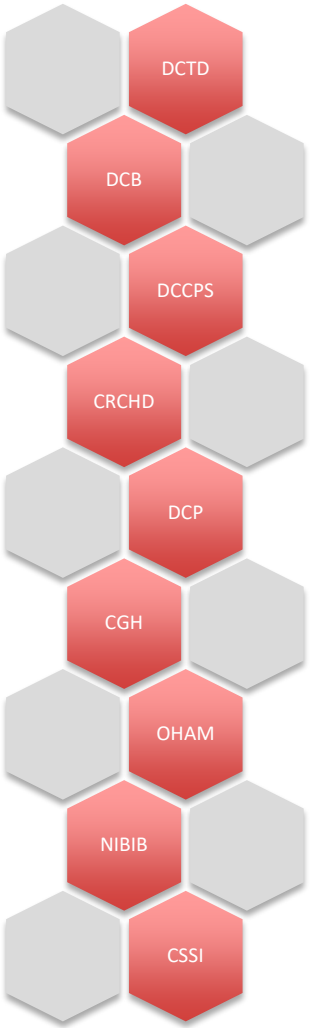
NCAB Ad-Hoc Subcommittee on Global Health

November 2017

Sudha Sivaram, PhD
NCI Center for Global Health

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

Trans-NCI and NIBIB Effort



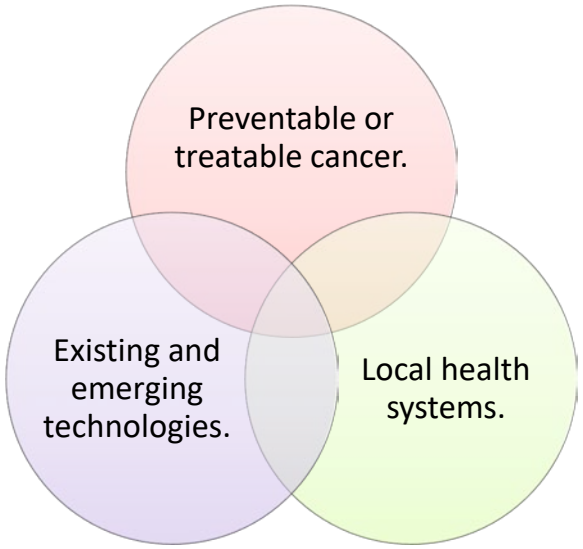
Result of collaboration by PDs across the the DOCs to identify priority areas and manage grants.

Critical Elements

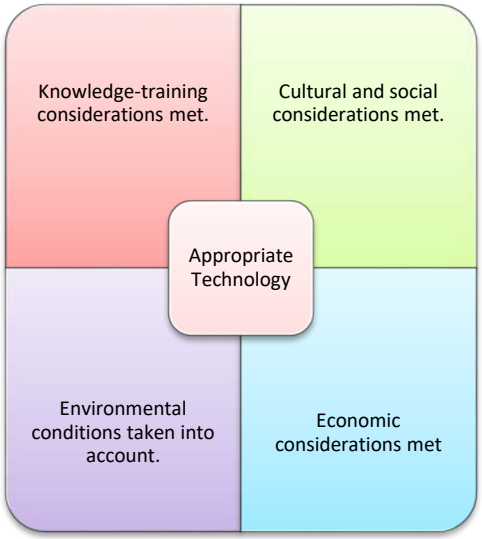
- Two-phase cooperative agreement.
- NCI BSA approved three Rounds: Awards run until 2022.
- **Phase I (UH2) - two years:**
  - Demonstrate clinical potential in a global health setting
- **Phase II (UH3) - three years:**
  - Validate device in global health setting
- **Progression from UH2 to UH3:**
  - Grantee must meet specified milestones
  - Milestones reviewed by NCI program staff.

NIBIB NATIONAL CANCER INSTITUTE
National Cancer Institute

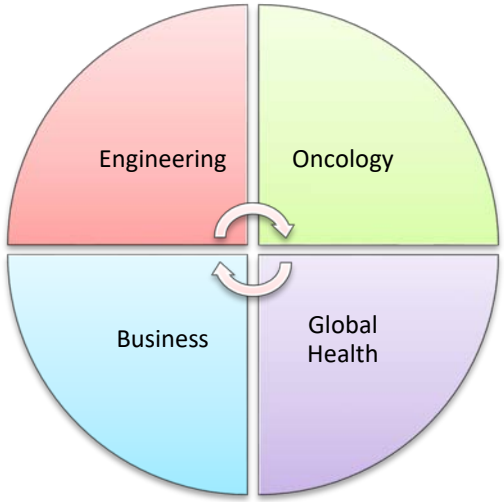
Scope



Focus



Teams

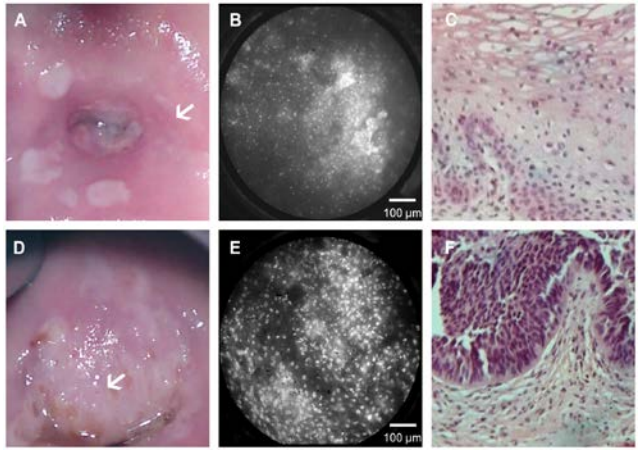


Grants from 1st Round

Funded Projects: Cervical Cancer Prevention and Diagnosis

- Adapting the Cepheid GeneXpert test to detect HPV
  (Louise Kuhn, Columbia – PD: Rao Divi)
  - Country proposed for UH3: South Africa
  - Technology: PCR

- High resolution micro-endoscopy for cervical cancer diagnosis
  (Kathleen Schmeler, MD Anderson
  and Rebecca Richards-Kortum, Rice – PD: Pushpa Tandon)
  - Country proposed for UH3: Brazil
  - Technology: Optical Endoscopy



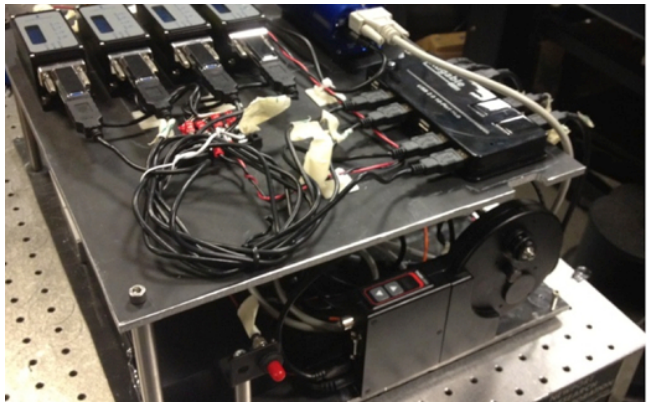
Funded Projects: Cervical Cancer Treatment

- Adaptation and testing of the CryoPen cryotherapy device for treating cervical neoplasia for use in LMICs
  (Miriam Cremer, Basic Health International– PD: Miguel Ossandon)
  - Countries proposed for UH3: Peru & Columbia
  - Technology: Cryotherapy

- Assessing the performance, safety and efficacy of a new cryotherapy device using liquid CO2
  (Jean Anderson, Hopkins – PD: Brian Sorg)
  - Country proposed for UH3: Philippines
  - Technology: Cryotherapy

Funded Projects: Oral Cancer Treatment, HCC Prevention,

- Low-cost enabling technology for image-guided photodynamic therapy of oral leukoplakia
  (Jonathan Celli, UM Boston and Tayyaba Hasan, Massachusetts General Hospital – PD: Lokesh Agrawal)
  - Country proposed for UH3: India
  - Technology: Battery-powered PDT



- A low-cost test for hepatitis C virus to identify patients at risk for developing hepatocellular carcinoma
  (Robert Murphy, Northwestern University – PD: Rao Divi)
  - Country proposed for UH3: Nigeria
  - Technology: RNA Viral Load Test

Funded Projects: Breast Cancer Detection/Diagnosis

- Low-cost, portable computer-aided detection and diagnostic (CADD) tools for non-invasive screening of breast cancer patients
  (Susan Love, Dr. Susan Love Research Foundation – PD: Vinay Pai)
  - Country proposed for UH3: Mexico
  - Technology: Ultrasound/CADD

Grants from 2nd Round

The Radiation Planning Assistant for Radiation Planning in Low- and Middle-Income Countries

[**PD:** Vikram Bhadrasain (DCTD)]

- Software to improve quality of RT treatment plans & increase productivity.
- Automates several routine, but critical tasks performed by physicists.
- UH2 Phase: Finalize development of tool at MD Anderson with some initial testing by partners in the Philippines and South Africa
- UH3 Phase: Deployment and evaluation.

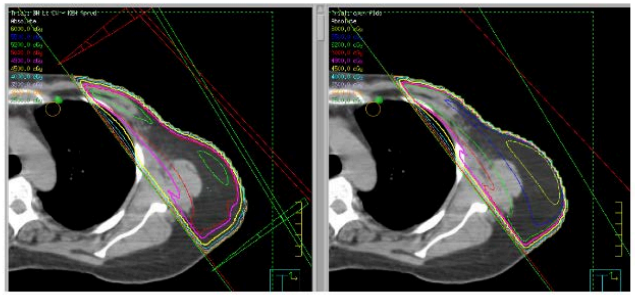


Figure 2. Comparison of the dose distribution for a chest wall treatment with optimized wedges (left) and with open fields (right). The non-optimized plan has a large region of soft tissue receiving 60Gy (6000cGy), compared with 52Gy (5200cGy) in the optimized plan.

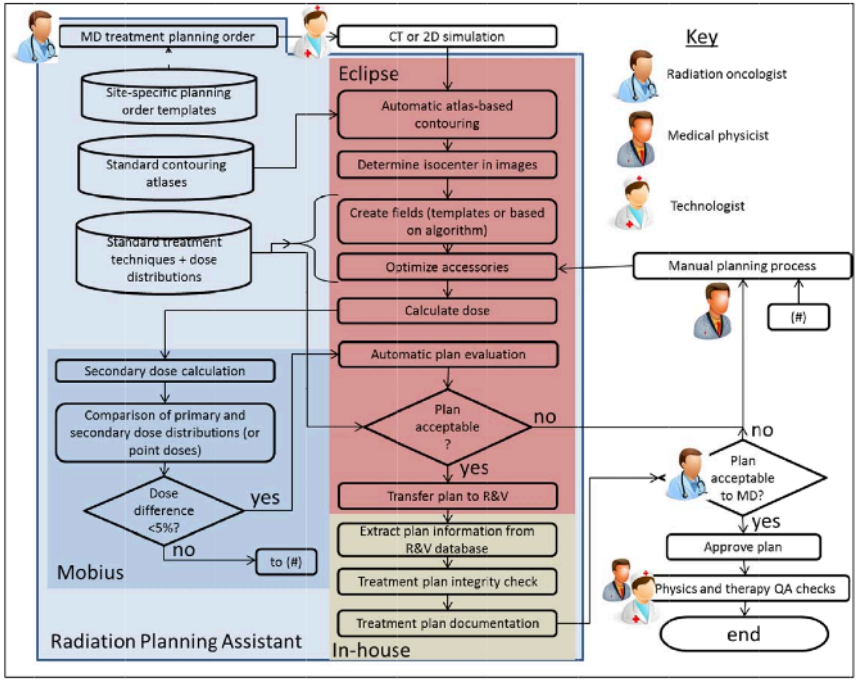


Figure 3. Radiation Planning Assistant process flow. The goal is that once the CT or 2D simulation images are passed to the Radiation Planning Assistant system, no more user interactions are performed until the plan is ready. Some data transfer (e.g., to the record-and-verify [R&V] system) likely requires some user input, although we will work to minimize this. Most of the steps shown here also have parallel steps in which the same processes are carried out independently. These parallel steps are used as QA checks.

Smartphone for Molecular Cancer Diagnostic In Africa

[**PD:** Rebecca Huppi (OHAM)]

- Holography-based molecular detection on a smartphone
  - FNA added to array chamber with lyophilized antibody coated beads of unique sizes/holographic signatures
- Bead binding is holographically measured using smartphone camera
- Image processing (cloud server) to quantify malignant cell count and subtypes
- Proposed for rapid, POC lymphoma diagnostics
- UH2: Initial validation studies
- UH3: Two trials in Botswana

Fig. 1. Photos of an iPhone hologram system (top) and its current control App (bottom).

Cytology-Free POC Cervical Cancer Diagnostics for Global Health

[**PD:** Miguel Ossandon (DCTD)]

- Multiplexed assay platform developed commercially by BD adapted for a highly-specific diagnostic test for cervical cancer.
  - Based on SERS technology, which enables detection of multiple targets without need for washing or purification.
  - Propose Detection of HPV (E6 and E7) for high sensitivity, and host response proteins (p16, Ki67, p14ARF) for high specificity
  - Test and analysis less than 30 minutes
- UH2: Adapt prototype/gather initial data
- UH3: Studies in Kenya, China, and Brazil

Figure 4: Lab-bench HNW instrument prototype that performs magnetic pelleting and Raman read on a single sample. Instrument is controlled via an attached laptop.

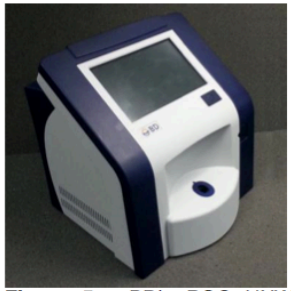


Figure 5: BD's POC HNW instrument for low resource settings. Instrument is controlled via an on-board CPU.

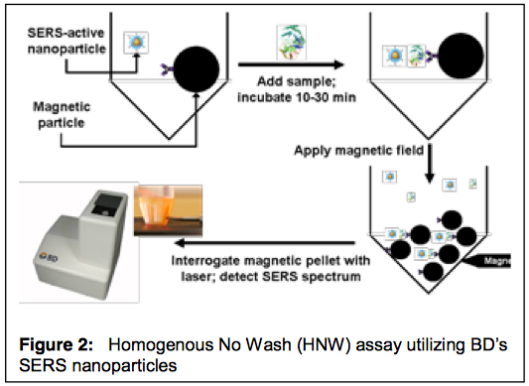


Figure 2: Homogenous No Wash (HNW) assay utilizing BD's SERS nanoparticles

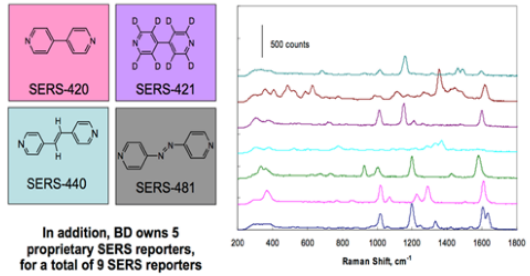
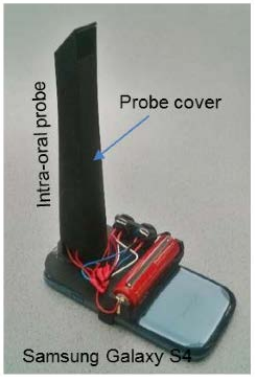


Figure 3: Left: BD has developed a suite of nine distinct SERS reporter particles, and has demonstrated the ability to spectrally unmix all 9 reports allowing for substantial multiplexing capabilities. Right: Examples of different Raman spectra from different flavors of SERS tags.

Low-cost Mobile Oral Cancer Screening for Low Resource Setting

[**NIBIB funding – PS:** Rao Divi (DCCPS)]

- Auto-fluorescence based mobile intra-oral imaging system.
  - Smartphone attachment.
- Allows for on-site clinical decision support.
- UH2: Further improvement/ruggedizing
- UH3: Validation for clinical utility in India



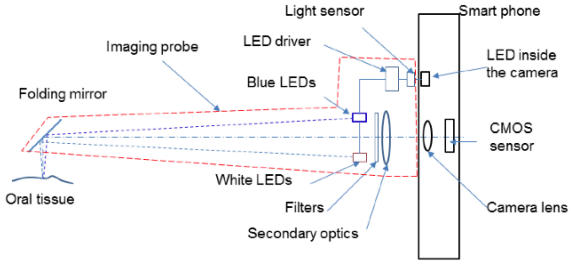


Fig. 13. Optical concept of the proposed mobile phone imaging device for oral cancer screening. All components in black are built-in components in mobile phone, others inside the red box are components in the intra-oral imaging probe. The phone is rotated 90 degree for concept demonstration.

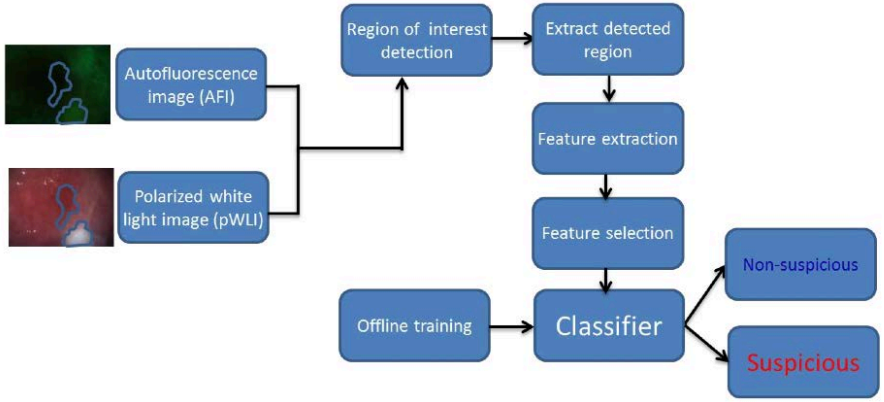


Fig. 14. The image processing approach to classify "Suspicious" and "Non-suspicious" regions.

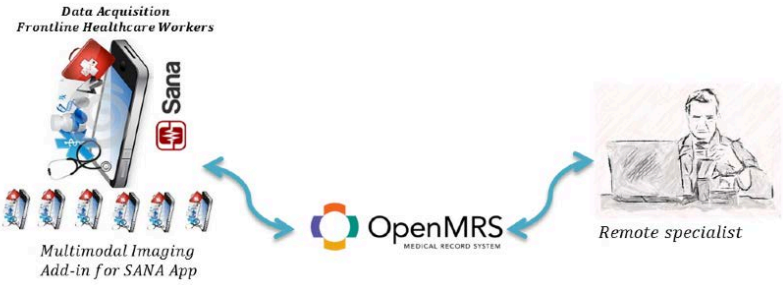
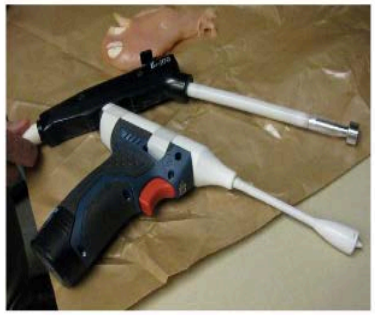


Fig. 15. The workflow of the mobile oral cancer screening application.

Development, field testing and evaluation of the efficacy of a hand-held, portable and affordable thermo-coagulator to prevent cervical cancer in low- and middle- income countries

[**PD:** Houston Baker (DCTD)]

- Goal is to develop, test, and produce 200 lightweight hand-held, cordless, portable, battery-driven and rechargeable thermal coagulators.
- UH2: Produce the 200 units. Modify device for
  - Fiber-optic lighting in vagina
  - Auto-sterilization
  - Anti-stick probe tip
- UH3: RCT to determine efficacy and user satisfaction.



A prototype of the thermal coagulator and a current cryosurgery device for size comparison. The thermal coagulator is cordless.

Development and clinical validation of a multi-type HPV E6/E7 oncoprotein test for cervical cancer screening and triage in low- and middle-income countries

[**PD:** Christos Patriotis (DCP)]

- OncoE6/E7 cervical test identifying E6 and E7 oncoproteins of HPV 16,18,31,33,35,45,52,58.
- Goal is to develop and validate this test in the context of the ESTAMPA study
- UH2: Analytical validation using randomized, histologically confirmed samples
- UH3: Clinical validation to determine efficacy for detection of HSILs and triage for colposcopy.

- There is a co-PI from Arbor Vita, the company that developed the test and a successful SBIR grantee.

Figure 3. ESTAMPA Research Network

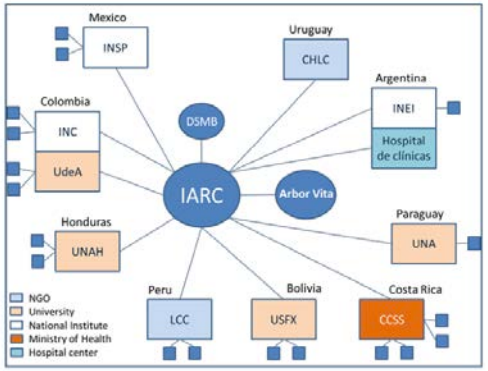


Figure 2. Onco*E6*™ Cervical Test – Adaptability

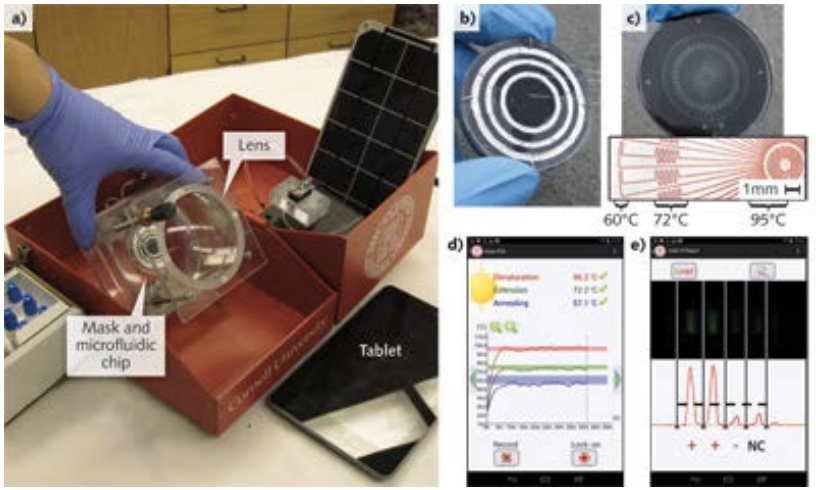
A) Onco*E6*™ Cervical Test unit **B) Work station setup** **C) Test result**

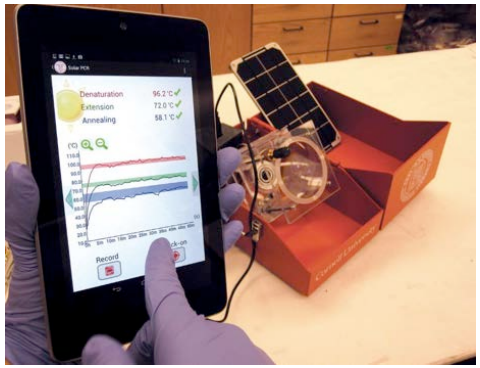
The OncoE6™ Cervical Test unit is moved from vial to vial on the rack to account for the different steps of the work flow: lysis, run, wash, and development (A). Equipment and footprint needed to run the test (B). Interpretation via visual inspection, aided by the Reading Guide. Line "C" represents a control for proper lateral flow run performance (C).

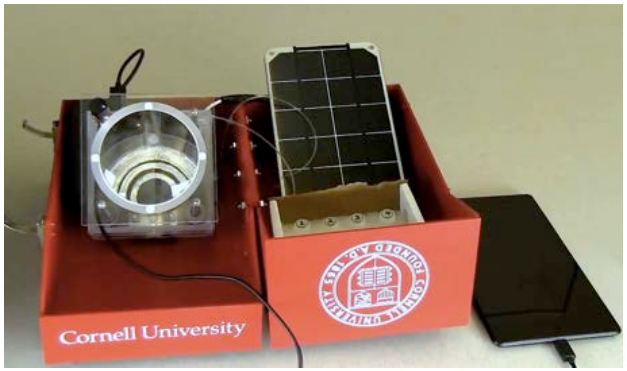
CA202723: Early Stage Diagnosis of Kaposi's Sarcoma in Limited Resource Settings Using KS-Detect

[**PD:** Rebecca Huppi (OHAM)]

- KS-Detect
  - Thermo-solar PCR used for molecular confirmation of KS in resource-poor settings.
  - Process involves converting sunlight into patterned heat and then using that heat to perform microfluidic processes (i.e., PCR).
  - Device is quasi-autonomous, easy to operate, and does not require any external energy input beyond ambient sunlight.







3rd Round

A cost-effective radiation treatment delivery system for LMICs

Eric Ford, University of Washington

- Goal: Develop cost-effective system for delivering RF that will provide IMRT at low cost.
  - Achieved using physical compensator adaptable to Cobalt-60 devices and linear accelerators.
- Has potential to improve the delivery of quality radiation in LMIC settings.

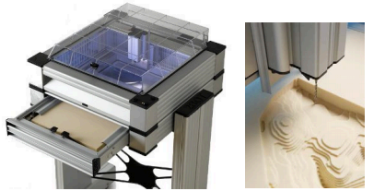


Figure 8: Desktop milling device for use in making physical compensator molds. The resolution is controlled by the size of the material subtraction bit (right panel).

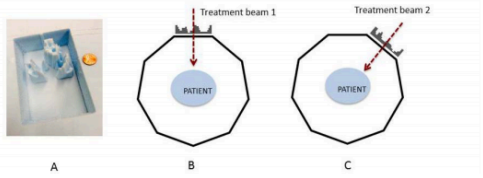


Figure 9: Schema for the use of compensators. **A:** compensator molds of foam or plastic are cut. Shown here is a prototype mold made on the machine shown in Figure 8. **B:** At the time of treatment a mold filled, with tungsten beads, is moved into position and the beam is treated. **C:** The device rotates to the next treatment angle. The next compensator is loaded and the next beam is treated. The process continues until all beams are treated.

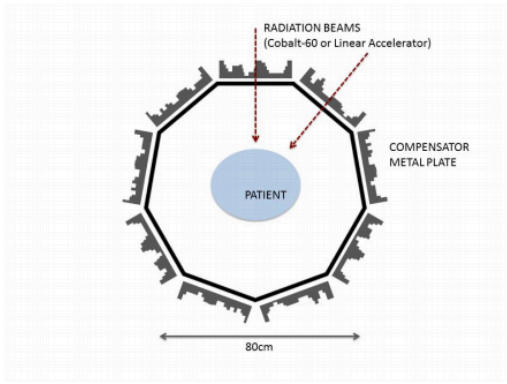


Figure 3: Proposed design to enable high-efficiency Intensity Modulated Radiation Therapy (IMRT). Physical compensators (plates filled with reusable tungsten pellets) are arranged in a compensator ring around the patient. Because staff do not need to enter the radiation vault between beams this system provides for extremely efficient treatment delivery.

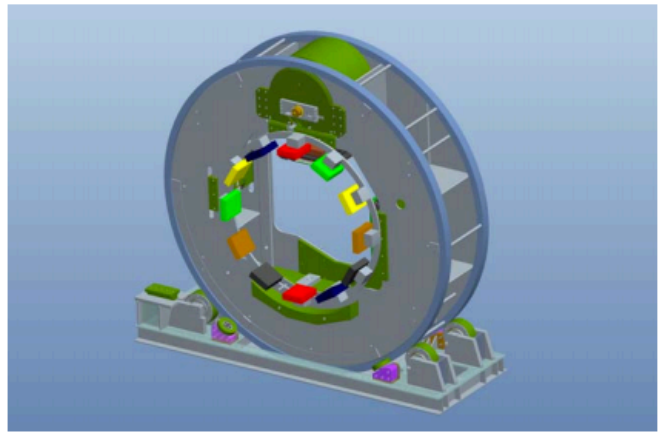


Figure 5: Prototype ring modulator system developed by the commercial partners, Panacea Medical Technologies Pvt. Ltd. (Bangalore, India). The treatment head and compensator exchange system is shown at the top (green).

Point of care, real-time urine metabolomics test to diagnose colorectal cancers and polyps in LMICs

Peter Kingham, Memorial Sloan Kettering

- Goal: Develop and validate a POC urine-based metabolic test for the diagnosis of patients with early stage of colorectal cancer and/or precancerous polyps.
  - Reduce the negative colonoscopy rate.
- Due to cost & practitioner knowledge/training gaps (1) colonoscopy as first line screening is impractical; (2) stool DNA tests are too expensive and lack of a POC option; and (3) other stool tests based in fecal occult blood are not optimal due to high prevalence of benign rectal bleeding.
- While proposed PolyDX test measures only indirect markers, test is likely prognostic will have a high impact on the field.

Figure 7. Rendering of a casing for the biosensor device, combining the electronic components, an electrode chip slot, and a smartphone for control.

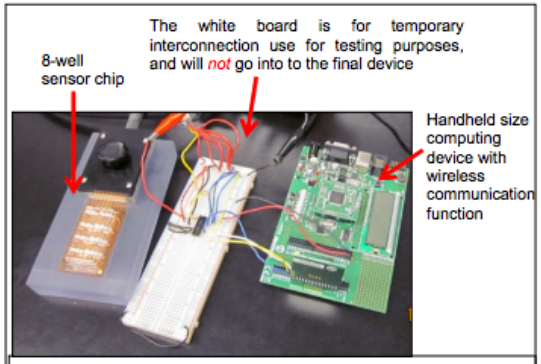


Figure 13. Photo of biosensor without its housing unit. The sensor chip is where the urine analysis is performed. The circuit board holds impedance measurement, result computing, Wi-Fi, and results display.

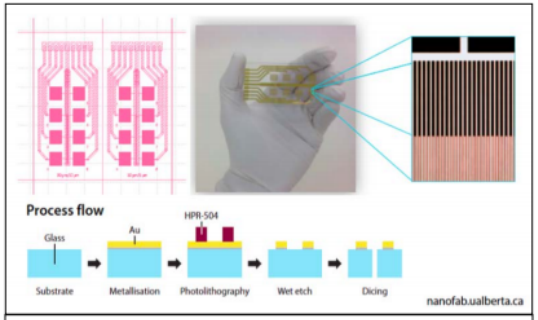


Figure 10. Sensor chip developed by Dr. Chen's team at the Nanofabrication Facility at the University of Alberta and the process flow, for reference.

Rapid POC Detection of HPV-Associated Malignancies

Karen Anderson, Arizona State University

- Goal: Develop multiplexed fluorescent POC assay for simultaneous detection of 16 individual HPV-specific serologic biomarkers from a finger stick blood sample, which can be manufactured for a reagent cost of less than $1/patient sample.

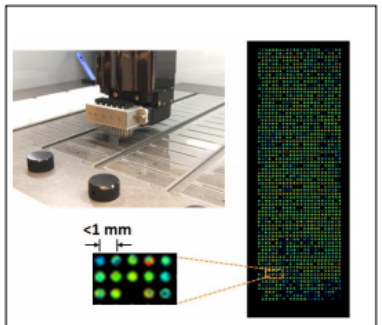
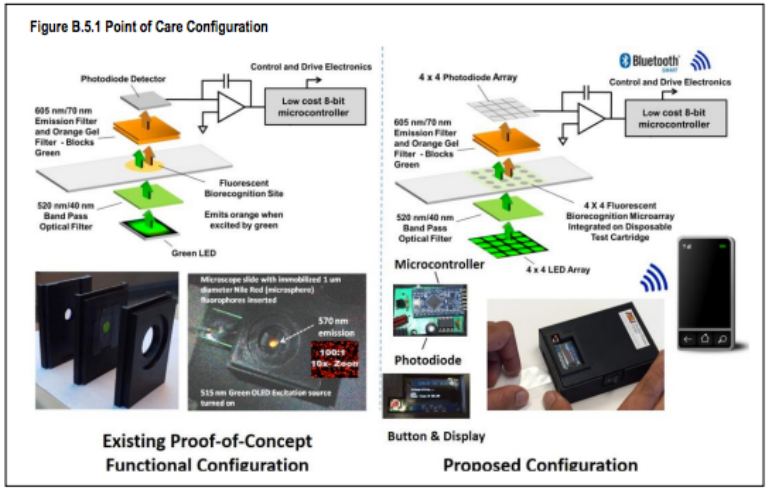


Fig. B.5.3.1 Micro-scale printing of high sensitivity fluorescent biorecognition protein microarrays at the ASU Biodesign Institute.

- Blood-based diagnostic
  - Appealing due to ease of use and popularity among patients.



- Work will leverage PI's decades of biomarker experience and POC assay work being performed under the NSF/NIH Smart and Connected Health program.

- This is a true POC medical diagnostic for HPV and will have potential to fundamentally change the HPV screening paradigm in low-resource settings.

Facile screening for esophageal cancer in LMICs

Stephen Meltzer, Johns Hopkins

- Goal: Develop single-use, swallowable sponge to collect esophageal specimens coupled with smartphone-manipulated microfluidic chip for automated sample processing and DNA methylation detectionfor early detection of esophageal squamous cell carcinoma.

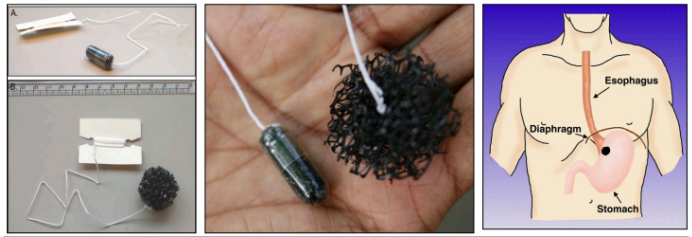


Figure 5. The CapNostics EsophaCap™ Swallowable Sponge. The collapsible plastic sponge is tethered to a filament and compressed within a soluble gelatin capsule. The end of the filament is held outside the mouth while the capsule is swallowed. Once inside the stomach, the capsule dissolves in a few minutes and the sponge expands. It is then retrieved by pulling on the filament. Cytologic material attaches to the sponge during exit, including cells from ESCC.

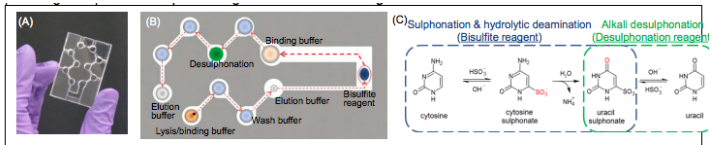


Figure 12. Droplet chip device for DNA bisulfite conversion. (**A**) A photograph of the device. (**B**) Layout of the chip. (**C**) Bisulfite conversion chemistry[73].

- In LMICs the 5-year survival is less than 10%. Uganda, where work will take place is located in an endemic area for ESCC which ranks the 3rd and 4th most-frequent cancer among males and females, respectively.
- Procedure can be administered by healthcare workers without medical degrees.
- Technology could be applied to other diseases by changing biomarker and sampling approach.

Digital PCR quantification of BCR-ABL for CML diagnosis and monitoring in a LMICs setting

Daniel Chiu, University of Washington

- Goal: Development of a digital PCR instrument for settings to detect BCR-ABL transcripts from blood samples to identify CML patients who are eligible for TKI therapy.

- GIPAP provides Gleevec at no cost to patients in LMICs. Challenge is selecting/ monitoring of patients with the BCR-ABL mutation that are candidates for the TKI.

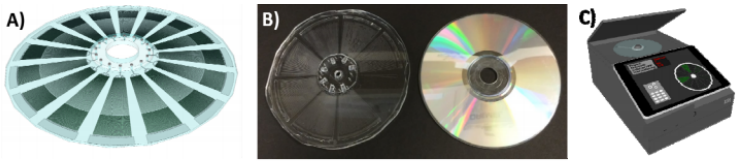


Figure 3: SD instrument and device prototype. *(A) Schematic showing SD disc design consisting of 16 arrays (i.e. for 6 patient samples where we run BCR-ABL and ABL each on a separate array plus 4 additional arrays for controls) for carrying out the BCR-ABL assay described in this proposal.* ***(B)*** *An image of an actual OD (optical disc) sized microfabricated SD device next to a commercial CD disc.* ***(C)*** *A hypothetical SD instrument capable of loading, thermal cycling, and imaging, with control via a tablet interface.*

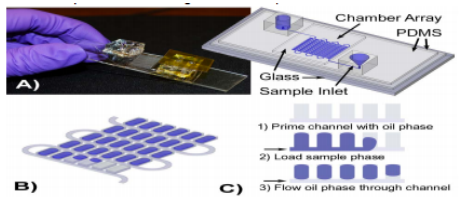


Figure 4: Components of the digital RT-PCR self-digitization chip. *(A) Image of assembled device with sketch of chip components.* ***(B)*** *Schematic of serpentine chip design used for single-cell experiments. Actual devices contain 1020 wells.* ***(C)*** *SD Chip filling mechanism.*

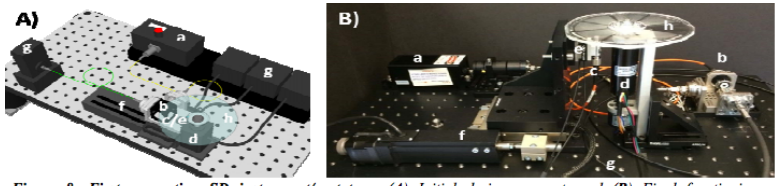


Figure 8: First generation SD instrument/prototype. *(A) Initial design concept, and* ***(B)*** *Final functioning instrument, with (a) laser, (b) fiber bench to hold optical components and filters to enable fluorescence imaging, (c/e) objective, and focusing stage, (d) rotary motor and encoder with mount, (f) linear stage and mount, (g) control/detection units and/or cables to the units, and (h) the OD scale device.*

- Project will create a low cost, field-deployable instrument capable of more precise quantification than standard RT-PCR at low template concentrations.

- When manufactured at scale, it is anticipated that the cost of the dPCR instrument will be < $1000 USD each with the cost of each SD chip at < $1.

Smartphone Enabled Point-of-Care Detection of Serum Markers of Liver Cancer

Ashutosh Chilkoti, Duke

- Goal: Develop a scalable and sustainable approach for early blood-based POC screening for HCC in LMICs.

  The highest HCC rates are found in LMICs, with >50% of all worldwide cases occurring in China and this technology will have broad impact by offering an affordable, scalable, and sustainable approach to screening.

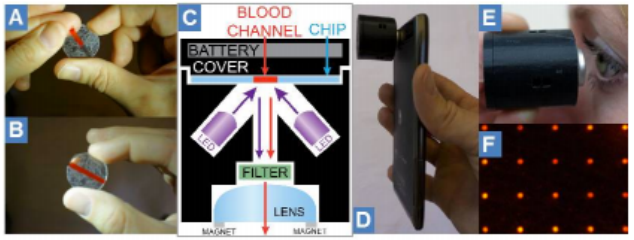


Fig. 13: 2nd generation D4 POCT. (A, B) The channel is created by two POEGMA-coated coverslips. Abs are printed on the bottom coverslip, in the center of the channel. Blood loads into the channel and is retained by capillary action. **(C)** Cutout schematic of the D4 detector. **(D)** Magnetic coupling/alignment of detector to smartphone **(E)** Visual examination of the signal **(F)** Digital photograph of a fluorescent test Ab array.

- D4 POCT only requires only a small finger stick of blood; there is no cold-chain required; assay chips are stable for at least 3 months at ambient temperature; and large scale production of chips will drive cost to <10 cents per assay.

Field-deployable platform for prognostic hepatic cancer screening in low-resource settings

Marc Porter, University of Utah

- Goal: Develop a quantitative vertical flow assay (qVFA) that simultaneously measures levels of 5 molecular markers of HCC risk in serum.

  qVFA will be optimized to deploy in PON settings in Mongolia, the country with highest HCC incidence in the world.

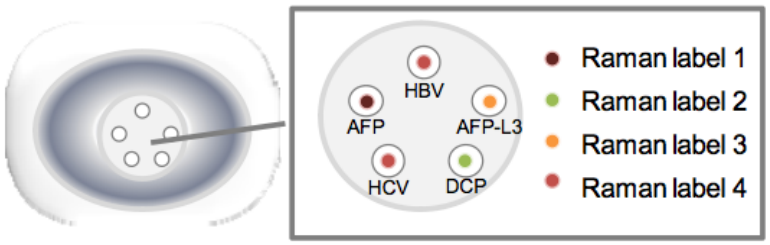


Figure 3. Proposed q-VFA format for a multi-analyte screening test to assess HCC risk.

Figure 4. *TacticID* handheld displaying an actual spectral readout of VFA membrane for AFP detection.

- Japan has demonstrated successful implementation of a program that incorporated the markers included in the qVFA (~85% sensitivity/~95% specificity) but at high cost. Production of the 5-plex qVFA HCC test is expected to be ~$2.5 and cost per patient ~$5.

- HCC can be controlled and survivability can be markedly improved if at-risk individuals can be identified earlier in cancer progression..

Drug Access Programs in Sub Saharan Africa

NIH NATIONAL CANCER INSTITUTE

African Access Initiative: BIO Ventures for Global Health

- Collaboration between
  - BVGH
  - African Organisation for Research and Training in Cancer (AORTIC)
  - IFPMA
  - Pfizer
  - Takeda
- Aim: To partner with companies, governments, healthcare providers, and NGOs focused on sustainably expanding access to cancer medicines and technologies, improving healthcare infrastructure, and building clinical and R&D capacity in Africa.
- Target countries in the Sub Saharan Africa Region: Cameroon, Cote d'Ivoire, Kenya, Nigeria, Rwanda
- https://bvgh.org/bio-ventures-global-health/african-access-initiative/

Access Accelerated Initiative: Pfizer

- Collaboration between
  - Pfizer
  - American Cancer Society
  - Clinton Health Access Initiative
- Aim: To provide access to critical cancer treatments such as chemotherapies. ACS and CHAI have negotiated on behalf of the target countries for Pfizer to offer competitive prices for eleven high-quality cancer treatments (9 are on the WHO's Essential Medicine List) through Government tenders and procurement mechanisms.
- Target countries in the Sub Saharan Africa Region: Ethiopia, Nigeria, Tanzania, Kenya, Uganda and Rwanda
- https://accessaccelerated.org/initiative/increased-access-cancer-treatments-africa/

Access Accelerated Initiative: Novartis GIPAP Program

- Collaboration between
  - Novartis
  - Axios International
  - Chinese Charity Foundation
  - Max Foundation
- Aim: To address the lack of access and reimbursement for cancer treatment in low- and middle-income countries. One of the largest programs is the Glivec International Patient Assistance Program (GIPAP) for patients with CML (chronic myeloid leukemia) or GIST (gastrointestinal stromal tumor).
- Target countries in the Sub Saharan Africa region: Angola, Benin, Burkina Faso, Cameroon, Cote d'Ivoire, DRC, Ethiopia, Gabon, Ghana, Kenya, Madagascar, Malawi, Mali, Mauritius, Niger, Nigeria, Rwanda, Senagal, Seychelles, Sierra Leone, South Africa, Tanzania, Togo, Uganda, Zambia, Zimbabwe
- https://accessaccelerated.org/initiative/novartis-oncology-access-programs/

Access Accelerated Initiative: Novartis Breast Cancer Program

- Collaboration between
  - Novartis
  - Boston University
  - Kenya Ministry of Health

  & Management Sciences for Health
  - Mission for Essential Drugs and Supplies
  - Red Cross
- Aim: To make available a portfolio of 15 critical chronic disease medicines to treat type 2 diabetes, cardiovascular diseases, respiratory illnesses, and breast cancer. These medicines are offered as a basket to governments, non-governmental organizations (NGOs) and other public-sector healthcare providers for USD $1 per treatment, per month. The aim is to make this innovative approach commercially sustainable over time, enabling continuous support in those regions.
- Target country in the Sub Saharan Africa region: Kenya
- https://accessaccelerated.org/initiative/novartis-access/

Access Accelerated Initiative: Roche

- Collaboration between
  - Roche
  - Beth Mugo Cancer Foundation
  - Kenya Ministry of Health
- Aim: To provide access to breast cancer medicine to patients seeking treatment at public institutions with the government of Kenya and Roche jointly covering the costs.
- Target country in the Sub Saharan Africa Region: Kenya
- https://accessaccelerated.org/initiative/combating-cancer-in-kenya/

Agenda

- NCI Leadership
- Global pediatric cancer
- Working with NCI-designated Cancer Centers
- Affordable Cancer Technology
- Improving access to cancer drugs in Africa
- New business