“Research Capacity Building in Latin America: The United States – Latin America Cancer Research Network Model”

Jorge Gomez, M.D., Ph.D.
Center for Global Health
National Cancer Institute
Guiding Principles

- Working with Latin America will provide **new insight** into cancer trends among the growing Hispanic population in the United States.

- Fostering **collaborations** based on mutual respect of the cultures, nuances, laws and regulations of each country will promote stronger partnerships with Latin America.

- Initiating research projects based on common interests and high bioethical standards will elevate the quality and credibility of cancer research conducted in Latin America and **advance science**.

- **Building research capacity** in Latin America will lead to independent, sustainable infrastructure to support first-rate clinical research around the globe.
A New Model for International Cancer Research

A bi-lateral agreement (LOI) among governments was signed in September 2009 where all governments “intend to enhance and expand cooperative efforts in the field of public health, medicine, science and cancer research”.

Connecting at the government, institution, and investigator levels

Provide a framework to encourage bilateral cooperation in addressing issues and problems of importance in the fields of public health, medicine, science and cancer research.

Colombia, Peru, and Puerto Rico were added in 2012.
“Molecular Profiling of Stage II and III Breast Cancer in Latin American Women Receiving Standard of Care Treatment (MPBC Study)”
Primary Objective of the MPBC Study

To characterize the distribution of invasive breast cancer stage II and III molecular subtypes (luminal A, luminal B, HER2-enriched, basal-like) in Latin American women.
Secondary Objectives of the MPBC Study

- To find association between molecular subtypes and tumor histopathologic characteristics prior to treatment including histological type, size, lymph node involvement, and surrogate markers

- To estimate pCR rate to standard neoadjuvant CT in each subtype – Residual cancer burden (RCB) index will be used to evaluate partial pathologic response to therapy
Secondary Objectives of the MPBC Study cont.

- To determine overall survival (OS), time to first failure (TFF) and disease-free survival (DFS) for each molecular subtype
- To document the demographic and epidemiologic characteristics of each subtype
- To discover and develop predictive and prognostic gene expression signatures
United States-Latin America Cancer Research Network (US-LA CRN)

US-LA CRN Governance
A New Model for International Cancer Research

Steering Committee

United States-Latin America Cancer Research Network

- Basic Research & Applied Technologies
- Pathology
- Biobanking
- Bioethics & Intellectual Property
- Informatics & Data Management
- Breast Cancer Surgery
- Clinical Oncology
- Epidemiology
- Communications
## Site and Participant Enrollment Status

<table>
<thead>
<tr>
<th>Sites/Accrual</th>
<th>Total Projected</th>
<th>Active/Current</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruiting Sites</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td>Basic Research Sites</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Biobanks</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Patient Accrual</td>
<td>3,000</td>
<td>~ 700</td>
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Pathology, Molecular Biology and Biobanking Procedures Standardization

- SOPs developed through a process of feasibility assessment, discussion and consensus with the Latin American investigators taking into consideration local practices, regulations, and capabilities to ensure sustainability.

- Annotation of quality parameters to capture relevant pre-analytical variables affecting blood, tissue and RNA quality.

- Biobank operations following the International Society for Biological and Experimental Repositories (ISBER) 2008 Best Practices and OBBR, NCI Best Practices.
Pathology, Molecular Biology and Biobanking Procedures Standardization (cont.)

- Self-monitoring:
  - Departure from SOPs (deviations and violations) and corrective actions
  - Impact on biospecimens quality and study data

- Single vendor for IHC/ISH reagents following ASCO/CAP recommendations

- Intra-country Proficiency Testing and external College of American Pathologists Proficiency Testing
Pathology, Molecular Biology and Biobanking Procedures Standardization (cont.)

- SOPs for collection, handling, processing and storage of surgical resections, biopsies and whole blood
- Guidelines for biospecimens labeling, transport and storage
- SOPs for RNA extraction, DNA microarrays and QC
- SOPs for ER, PgR, HER2 and Ki67 IHC/ISH and interpretation of results following ASCO/CAP recommendations
- SOPs for pathologic response to chemotherapy - assessment by RCB index
Breast Cancer Molecular Profiling

DNA Microarrays for MPBC Study:

- Agilent 4x44 K array
- Biopsies (or surgical resections if biopsy not available) with more than 60% tumor cells and less than 20% necrosis per H&E
- Two-color fixed design
- RNA extraction and microarray SOPs
- Correlation with surrogate markers (IHC/ISH)

From Perou, Nature, 2000
Bioinformatics Platform

- Pathology, clinical, epidemiology, microarray, and biospecimen quality data stored in OpenClinica™ (open source clinical database management system) – available in 3 languages

- Biospecimen inventory and tracking in BSI-II™

- Annotated data on pre-analytical variables that affect blood, tissue, and RNA quality in OpenClinica™

- Ability to interface with other applications for statistical analysis

- Dashboard to automatically generate progress reports
Epidemiology Modules

- Socioeconomic and Demographics
- Access to health care services
- Cancer History
- Hormonal and reproductive history
- Medical history
- Tobacco/alcohol consumption
- Anthropomorphic factors and physical activity
Socioeconomic and Demographic

- Origin: country/region
- Self described ancestry
- Occupation/income
- Housing conditions/sanitation/water
- Schooling
Access to Health Services

• Health insurance/coverage
• Ca screening
• Bc screening/tests/age/frequency of mammograms/biopsies/surgeries/current Dx/visits
• Costs associated with Dx
Cancer History

- Number of pregnancies/multiple births
- Self described ancestry and parents
- Parents/grandparents/brothers/sisters cancer history/age/types
- Biological children/other relatives
Hormonal and Reproductive History

- Age at first menstrual period
- Number of pregnancies/age/# births
- Miscarriages
- Breast feeding
- Treatments to become/maintain pregnancies
- Birth control methods
- Menopause/treatment
Medical History

• History of other diseases, age, treatments, surgeries
Tobacco and Alcohol Consumption

- Smoking, frequency, number
- Former smokers
- Second hand smoking
- Drinking habits, frequency, type and quantity
- Age
Anthropomorphisic Factors and Physical Activity

• Height, weight
• Lightest weight, age
• Physical activity type (walk, bike, etc.)
• Workday activity
Free, open source clinical trial software for Electronic Data Capture (EDC) and clinical data management in clinical research

- Web-based & designed to support all types of clinical studies in diverse research settings
- caBIG compatible
- Designed to support regulatory guidelines such as US FDA 21 CFR Part 11 (electronic signatures and audit history)
- Reduces duplication of data, data entry errors
- Automates and streamlines discrepancy (data query) management and the clinical trials workflow
- Provides ability to export data into standard formats

www.openclinica.org
OpenClinica™ Features

- Management of many, diverse, clinical studies through a single interface
- Clinical data submission, validation, and annotation
- Data filtering and extraction
- Study oversight, auditing, and reporting
- Protocol configuration, design of Case Report Forms (CRFs)
- Electronic Data Capture (EDC), retrieval, and clinical data management
Functional Areas of the Application

Submit Data
Allows subject enrollment, data submission and validation for use by clinicians and research associates as well as Query Management and Bulk Data Import.

Monitor and Manage Data
Enables ongoing data management and monitoring of clinical trials

Extract Data
Enables data extraction and filtering of datasets for use by investigators

Study Build
Facilitates creation and management of studies (protocols), sites, CRFs, users and study event definitions by investigators and coordinators

Administration
Allows overall system oversight, auditing, configuration, and reporting by administrators
Impact of the MPBC Study - Summary

- Collection of high-quality, well-annotated biospecimens to permit future collaborations and increase scientific knowledge

- Creation of a systematic model for conducting cancer research in Latin America: multidisciplinary team of Latin American investigators to participate in study conception, design, analysis, monitoring, reporting, and publication

- Improvement of breast cancer diagnosis by following standard procedures and attending highest quality standards for IHC and FISH

- Gaining a better understanding on the correlation of BC molecular profiles with response to therapy and survival in Latin American women → potential impact on treatment recommendations
The Value of Collaborating in Latin America

- Highlights the importance of reaching beyond borders
- Demonstrates the benefit of Latin American cancer research in improving care for the growing Hispanic population in the United States
- Leverages countries’ resources and breaks down research silos
- Enhances research capabilities in Latin America and the U.S. for global benefit
- Improves state of the science
- Provides the opportunity for NCI to have significant impact in the United States and abroad
Global Health as an NIH Priority

“Global health research ‘should be a conversation with other countries,’ but not one in which the great ‘United States tells the world what the answers are without listening to their experiences’.”

Remarks of NIH Director Francis Collins
FIC’s Global Health Matters Newsletter
NIH “Town Meeting”
August 17, 2009
Project Management & Scientific/Technical Support
Jorge Gomez, NCI, CGH
Teri Brown, NCI, CGH
Elizabeth Baseler, SAIC-F
Silvina Frech, SAIC-F
Mariana González del Riego, SAIC-F
Mark Cosentino, SAIC-F
Norma Diaz-Mayoral, SAIC-F
Caroline Sigman, CCSA Inc
Donya Bagheri, CCSA Inc
Kisha Thomas, CCSA Inc

Scientific/Technical Consultants
Federico Monzon, Baylor College of Medicine
Charles Perou, University of North Carolina at Chapel Hill
Katherine Hoadley, University of North Carolina at Chapel Hill
James Robb, consultant
Claudine Isaacs, Georgetown University
Beth Jones, Yale School of Medicine
Erik Ruuth, consultant
David Weiss, Agilent Technologies
Scott Vaccha, Agilent Technologies
Mickey Williams, SAIC-F
Fraser Symmans, M.D. Anderson Cancer Center
Michael Gilcreast, M.D. Anderson Cancer Center

Bioinformatics & Biostatistics
Daniel Milgram, CCSA Inc
Elizabeth Garret-Mayer, Medical University of South Carolina
Don Young, CCSA Inc
Kevin Meager, IMS
Jennifer Spahn, IMS
Sean Brennan, IMS
Jose Galvez, NCI, CBIIT

Research/Business Administration
Juan Tayco, NCI, CGH
Catherine Hidalgo, NCI, CGH
Calvin Proffitt, SAIC-F
Jen Imes, SAIC-F
Irene Mueller, SAIC-F
Matt DeSantis, SAIC-F
Silvia France, SAIC-F
Melanie Baker, SAIC-F
Olga Stabinger, CCSA Inc

Communications
Nelvis Castro, NCI, OCE
Nina Ghanem, NCI, OCE
Shannon Hatch, NCI, OCE

Latin American Investigators
Thank you!
¡Muchas Gracias!
Obrigado!