Session 2: UNC Lineberger and UCRF
Overview
H. Shelton Earp MD
May 25, 2011
UNC Lineberger: A Public Comprehensive Cancer Center

Basic research: Molecular, cellular, & animal model research

Clinical & Translational Research: Diagnostics & therapeutics

Clinical Care: Patient-centered excellence

Economic Development
Intellectual property
Attract & start companies

Dissemination & Outreach
AHEC, community & clinical practice, quality, anchor counties

Population Sciences
Epidemiology, prevention, early detection, minority disparities, & health Outcomes

UNC System Partners
East Carolina Univ., NC State, NC Central Univ.
UNC Charlotte
UNC Lineberger’s Strength
Integrating a Superb Faculty across a Great University

Research
315 Members
12th in NCI Funding
$220M Cancer-Related Funding
34 multi-investigator grants

Clinical
125,000 Patient visits
4,000 New patients
1,054 on therapeutic trials

Training
26 pre & post-doctoral training grants
Growth in High Impact Publications

<table>
<thead>
<tr>
<th>Journal</th>
<th># Pubs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell</td>
<td>37</td>
</tr>
<tr>
<td>Science</td>
<td>22</td>
</tr>
<tr>
<td>Nature</td>
<td>32</td>
</tr>
<tr>
<td>JAMA</td>
<td>19</td>
</tr>
<tr>
<td>NEJM</td>
<td>23</td>
</tr>
<tr>
<td>JNCI</td>
<td>30</td>
</tr>
<tr>
<td>AJPH</td>
<td>20</td>
</tr>
<tr>
<td>Nat Genet</td>
<td>29</td>
</tr>
<tr>
<td>Cancer Cell</td>
<td>16</td>
</tr>
<tr>
<td>PNAS</td>
<td>124</td>
</tr>
<tr>
<td>Genes &amp; Dev</td>
<td>18</td>
</tr>
<tr>
<td>Blood</td>
<td>49</td>
</tr>
</tbody>
</table>
Extraordinary Support from the State
Unique features of this exceptional Cancer Center include its outstanding institutional support that has created a research infrastructure and advocacy resulting in high impact scientific contributions.

The UCRF provides a unique wave of support with three clear goals: to improve cancer outcomes, use genomics in cancer research and to develop new cancer treatments. The center leadership views this resource stewardship as a central responsibility it has to the population of North Carolina.

The funding will be used to improve the lives of the population through improved understanding of cancer as a disease process linked to genetic risk, new druggable targets, novel clinical trials, and population based research that will better inform cancer prevention and early detection.

Overall, these efforts should improve the outcome of cancer for the residents of the state and the country and provide evidence that this center will remain an exceptional example of a matrix cancer center.

Exceptional
SWOT Analysis:
All good except $$

UCRF: Stable funding
NIH: A tougher environment
but UCRF gives competitive advantage
UNC Health Care: Unclear
UNC Lineberger/UCRF Strategic Plan

Tier III
- Optimizing NC Cancer Outcomes
- Cancer Genetics/Genomics
- Developing New Cancer Treatments

Tier II
- Opportunity Fund
  Innovation, Technology & Recruitment

Tier I
- Infrastructure
  Clinical Excellence & Outreach, Clinical/Translational Research Cores,
  Tissue Procurement & Informatics, Population & Basic Science Cores
UCRF Recruitment By Year

Updated May 2011
Clinical Excellence:

A prerequisite for our service and research mission
Growth in Multidisciplinary Care

- Bone & Soft Tissue
- BMT
- Breast
- Genetics
- GI
- GYN
- Urologic
- Thoracic
- Pediatrics
- Skull-Base Tumors
- Psycho-Oncology
- Leukemia & Lymphoma
- Pediatrics
- Ocular Tumors
- Head & Neck
- Brain Tumor
- Melanoma
- Head & Neck
- Geriatric Oncology
- Ocular Tumors
Recruitments
- Urologic Oncology
- Leukemia/Lymphoma/BMT
- Surgical, Medical Oncology
- Radiation Oncology
- Pediatric Oncology
- Neuro Oncology
- GYN Oncology

Platforms
- Tissue Procurement
- Clinical Protocol Office
- Psycho-oncology
- Telemedicine
- Clinical Trials Network
- Training

Infrastructure
- Clinical Excellence & Outreach
- Clinical/Translational Research Cores
- Tissue Procurement & Informatics
- Population & Basic Science Cores

Technology/Cores
- Translational Pathology Imaging
- Proteomics
- Basic Science Cores
- Biostatistics
- Clinical Informatics

Project Funds
- Clinical Innovation
Telemedicine Operation

• Tumor Boards -- Working Methods
  – Five active boards
  – Delivering information, scheduling, reporting
  – UNC Radiology receives remote images
  – UNC Pathology reviews slides from sites
  – Staff schedule and support remote sites

• Clinical Trials
  – Trial start-up meetings
  – Staff training

• Psycho-Oncology & Genetics Consultations
  – Rural areas

• Active CME Credit Hours
  – GI, Breast, Heme / Lymphoma, Head & Neck

• Radiation Oncology Education

• Bioethics(UNC, Duke, NC State)

• Protocol Review Committee
  – (UNC, ECU, Rex)

• Challenges/Opportunities
  – Stimulate utilization by practitioners
  – Scheduling for UNC faculty and community MDs
  – Use of centralized (hospital) vs smaller office sites
  – Use for consultation in rural areas

Brooke Burnworth, Michael Young, & Kari Hess

Equipment costs to date - $2M
Yearly operating costs - $350K
Need to expand faculty
UNC Lineberger Clinical Trials Network

Research Sites

A network in evolution
A variety of sites and capabilities:
Trials accrual
Prevention/survivorship research
Tissue procurement
UNC Lineberger Clinical Trials Network

- Functions:
  - Staff at UNC, Rex, and ECU
  - Initial visits, assess capability, negotiate master agreements
  - Correlative science – specimen storage
  - Contract vendor delivers investigational drugs
  - UNC Lineberger holds INDs

Key Staff:
Brian Kiley, Madlyn Ferraro, Joy Ostroff
Network Accrual

Investigator Initiated Trials | Cooperative Groups
---|---
CY2008: 142 | 59
CX2009: 64 | 160
CY2010: 309 | 62
Accrual to Therapeutic Trials

![Accrual to Therapeutic Trials Chart]

- **Institutional**
- **Industry**
- **National Group**
Recruitments
Health Communications
Minority Disparities
Outcomes
Public Health Interventions
Behavioral Science
Molecular Epidemiology
Quality of Life
Population Methodology

Platforms
CBCS III
Survivorship Cohort
ICISS

Core Resources
Community Engagement
Dissemination
Rapid Case/ State Registry
Health Communications

Optimizing NC Cancer Outcomes

Project Funds
HealthE NC
Overview: North Carolina as a Laboratory
Platforms for Quality of Care & Survivorship Research

• **UNC Hospital-based survivorship cohort**
  - Target accrual: 10,000 patients
  - Pretreatment epidemiologic and psychosocial data
  - Extraction of pathology, clinical, and treatment data
  - Germline DNA and genomic analysis of tumor samples
  - Yearly follow-up
  - Consent form allows reconsent for future studies
  - Potential co-development with SAS

• **ICISS (Integrated Cancer Information Surveillance Systems)**
  - State tumor registry data (44,500 cases yearly)
  - Claims data: Medicare, Medicaid, State, BCBS
  - BRFSS, Epidemiologic, GIS data, etc.
  - Understanding care and quality in the state
Survivorship Cohort: UNC & SAS

Federation not used for SAS partnership, but still used for future CDW-H / LDBR integrated data needs

ITS Research Computing established as the trusted hosting entity within UNC

Pending CDW-H / LDBR Federation

SAS team only have access to specific server(s) running their software, and no ability to remove data

Manual extraction of data from CDW-H and load to cancer data mart initially. Automated loads will be established once data requirements stabilized.

SAS Software

Secure Medical Workspace (SMW)

CDW-H Research Analyst

Extracted Data

ISD

P&A

OR

Etc.

CDW-H

Federated Data Network

Data Marts

LCCC

LCCC Data & Bio-specimen Repository (Genomics)

ITS Research Computing

Cancer Research Data Mart

HW Firewall

VPN

SAS
Carolina Breast Cancer Study: Phase III

- Population-based
  - Molecular etiology to clinical outcomes

- 3,000 cases
- 50% African American
- 50% under age 50
- Clinical follow-up in the community setting

Senator Jeanne Lucas
North Carolina: A Laboratory

Research
ICISS
Quality of Care
Comparative effectiveness
Outcomes – state-wide database
Prevention & early detection

Optimizing NC Cancer Outcomes

Disease-Specific Tumor Boards by Telemedicine
Sites: 18
Oncologist Offices: 28
**Recruitments**
- Cancer Genetics - Clinical
- Cancer Genetics - Discovery
- Pharmacogenetics
- Computational Biology
- Bioinformatics
- Molecular Pathology

**Platforms**
- Bioinformatics
- Next Gen Sequencing
- Collaborative Cross

**Technology/Cores**
- Clinical Genomics
- Data Management & Storage
- Informatics Pipeline
- High Throughput Sequencing
- Genome Sciences Up-Fit

**Project Funds**
- Cancer Predisposition Genes
- Clinical Sequencing
NCI Cancer Genome Atlas: Glioblastoma Subtypes

Integrated Genomic Analysis Identifies Clinically Relevant Subtypes of Glioblastoma Characterized by Abnormalities in PDGFA, IDH1, EGFR, and NF1

Roel G.W. Verhaak,1,2,3,4,5,6,7 Katherine A. Hoadley,3,4,7,8 Elizabeth Purdom,7 Victoria Wang,8 Yuan Q.1,8 Matthew D. Williamson,1,9,10 C. Ryan Brinckerhoff,10 Li Ding,11 Todd Golub,11,12,13 Jillip. Mostov,7 Gabrielle Alexe,1 Michael Lawrence,1,2 Michael O’Kelly,11 Pablo Tamayo,1 Barbara A. Wert,15 Tyson Gabriel,1 Wendy Weinberg,16 Suzy Gupta,1

1The Eli and Edythe L. Broad Institute of Massachusetts Institute of Technology and Harvard University, Cambridge, MA 02142, USA
2Department of Medical Genetics, Dana-Farber Cancer Institute, Boston, MA 02115, USA
3Department of Oncologic Sciences, University of Cincinnati, Cincinnati, OH 45267, USA
4Department of Biostatistics, University of Washington, Seattle, WA 98195, USA
5Department of Neurology, University of Washington, Seattle, WA 98195, USA
6Department of Radiation Oncology, University of Washington, Seattle, WA 98195, USA
7Department of Pathology, University of Washington, Seattle, WA 98195, USA
8Howard Hughes Medical Institute, Chevy Chase, MD 20815, USA
9Department of Pediatrics, University of Washington, Seattle, WA 98195, USA
10Department of Biostatistics, University of Washington, Seattle, WA 98195, USA
11Department of Pathology, University of Washington, Seattle, WA 98195, USA
12Department of Genetics, University of Washington, Seattle, WA 98195, USA
13Department of Pathology, University of Washington, Seattle, WA 98195, USA
14Department of Biostatistics, University of Washington, Seattle, WA 98195, USA
15Department of Medical Genetics, Dana-Farber Cancer Institute, Boston, MA 02115, USA
16Department of Medicine, Massachusetts General Hospital, Boston, MA 02114, USA

Chuck Perou, PhD
Lisa Carey, MD
Katie Hoadley, PhD

The Cancer Genome Atlas
Next Generation Sequencing and Bioinformatics

Neil Hayes, MD
**Recruitments**
Chemical Biology
Nanotechnology
Molecular Targets
Drug Discovery
Drug Delivery

**Platforms**
Chemical Biology
Nanoparticle Fabrication
Mouse Phase I Unit
Whole Genome Screening

**Technology/Cores**
Animal Studies & Models
Material Sciences
Structural Biology
RNAi Screening
New Venable Up-Fit
MEJ 10\textsuperscript{th} Floor

**Project Funds**
Interventional Oncology
Novel Anti-Angiogenics
Stephen Frye, PhD
Former head, GSK world-wide med chem
Center for Integrative Chemical Biology and Drug Discovery (CICBDD) NCI-funded Chemical Biology Drug Discovery Consortium

Bill Zamboni, PharmD, PhD
University of Pittsburgh
Translational Oncology and Nanoparticle Drug Development Initiative
GLP Analytic Facility

Developing New Cancer Treatments
Targeting Mutant IDH1

Normal cells

IDH1

ICT

IDH1

ICT

IDH1 mutated

ICT

IDH1 mutant

α-KG

Targeting IDH1 and IDH2 mutated glioma and AML

Cell-permeable α-KG to restore α-KG

α-KG

IDH1-2 mutation

αKG-dependent dioxygenases

2-HG

Inhibitors of mutant IDH1/2 to block the 2-HG

JmjC Histone Demethylases

Yue Xiong & Stephen Frye: IDH1 Drug Discovery Program

NExT funding
Center of Cancer Nanotechnology Excellence

$2M GO Grant

Imaging, therapeutics, & vaccines

Developing New Cancer Treatments
Recruitments
Tumor Immunology
Tumor Virology
Cancer Biology
Inflammation
Angiogenesis
DNA Recombination & Repair
Hematologic Malignancies

Technology/Cores
Renovations
Equipment Fund

Opportunity Fund
Innovation, Technology & Recruitment

Innovation Awards
<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>James Bear, PhD</td>
<td>Computer Vision-based Analysis of Tumor Cell Invasion and Adhesion</td>
</tr>
<tr>
<td>Andrew Dudley, PhD</td>
<td>Resistance to Anti-angiogenic Strategies by Tumor Cells with Features of Vascular Cells</td>
</tr>
<tr>
<td>Gary Johnson, PhD</td>
<td>Defining Kinome Activity for Novel Cancer Therapies</td>
</tr>
<tr>
<td>Larry Marks, MD</td>
<td>Reducing the Risk of Radiation-Associated Second Malignant Neoplasms for Long-Term Cancer Survivors</td>
</tr>
<tr>
<td>Matt Redinbo, PhD</td>
<td>Novel Therapeutics to Alleviate Anticancer Drug Toxicity</td>
</tr>
<tr>
<td>Bryce Reeve, PhD</td>
<td>Development and Pilot Test of the UNC Patient-Reported Symptom Monitoring (PRSM) System in the North Carolina Cancer Hospital to Enhance Quality of Cancer Care</td>
</tr>
<tr>
<td>Cyrus Vaziri, PhD</td>
<td>Inhibition of the DNA Repair Enzyme Rad18 as a Novel Strategy for Sensitizing Tumor Cells</td>
</tr>
<tr>
<td>Yue Xiong, PhD</td>
<td>Mechanisms and Drug Discovery for IDH Pathway in Gliomas</td>
</tr>
</tbody>
</table>
UCRF Innovation Awards

- To support innovative cancer research by UNC faculty and UNC Lineberger members
- Six rounds completed
  - 11/07, 6/08, 12/08, 11/09, 5/10, 12/10
- 372 applications, 64 awards, $10.3M awarded
- 17.2nd percentile; avg award $161,469 (2 yrs)
  - 15th percentile in 12/2010 round; $189,375 avg award (2 yrs)
- Peer review by more than 80 faculty
- Next round scheduled for summer 2011
Results from Round 1 (11/07)

- We made 18 awards for $2.4 million
- ~8:1 return in extramural grant funding
  - 23 awards, $20.4 million (total costs, all years)
  - 6 NCI R01s, 3 NIH R01s, 1 NCI R21, 2 NIH R21s, 1 NSF, 1 DoD IDEA award, 1 Komen award
- Other research products
  - 1 clinical trial
  - 2 ROIs filed
  - Contribution to 1 start-up company
Cancer as a Global Health Issue

• The number of global cancer deaths projected to increase 45% from 2007 to 2030 (from 7.9 million to 11.5 million deaths).

• New cases of cancer estimated to jump from 11.3 million in 2007 to 15.5 million in 2030.

• Already more than half of all cancer cases occur in developing countries.
UNC in Malawi and Tanzania
UNC Lineberger Global Oncology/AIDS Malignancy Program

A new initiative…

Blossom Damania, Leader

Dirk Dittmer, Core Resource Leader

Carol Shores, Malawi Project
Questions?