Building the Ohio Innovation Economy

Biomedical Grown Opportunities – Advances in Cancer Research

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Today’s Thoughts

♦ What is the cancer reality?
♦ How do we see and characterize the future of healthcare (read personalized medicine)?
♦ If disruptive innovation is our best hope – what areas represent opportunities/barriers?
♦ Are there current examples of high promise?
♦ And the future?
“...we can harness the historic convergence between life sciences and physical sciences that’s underway today, undertaking public projects in the spirit of the human genome project to create data and capabilities that fuel discoveries in tens of thousands of laboratories and identifying and overcoming scientific and bureaucratic barriers to rapidly translating scientific breakthroughs into diagnostics and therapeutics that serve patients...” (THE NOT ONE SIZE FITS ALL INNOVATION IMPERATIVE – WILL WE HARNESS CONVERGENCE?)

...Today, of course, we face more complex challenges than we have ever faced before, a medical system that holds the promise of unlocking new cures and treatments attached to a health care system that holds the potential for bankruptcy to families and businesses...” (THE HOW MUCH TECHNOLOGY CAN WE AFFORD QUESTION)
40th Anniversary: Official Launch of the U.S. “War on Cancer”

December 23, 1971, President Richard Nixon signs National Cancer Act

- 1969 – Full Page New York Times: “Mr Nixon You Can Cure Cancer”…Just lack the will and resources that put a man on the moon”
- Senator Yarborough: “…achieve cures for the major forms of cancer by 1976 – . bicentennial of the republic!”
Cancer Reality

- ~ 560,000 Americans will die of cancer this year
- ~ 1.5 million Americans will be diagnosed with cancer this year
- ~ $264 billion (economic burden of cancer in 2010 (ACS)
- New cancer cases will increase by 30-50% as we approach 2020
- ~ 65,000 new cancer cases in Ohio this year

Unlike Other Major Disease Killers, Cancer Continues to Take Nearly the Same Toll as it did in 1950

Source for 2006 deaths and diagnoses: American Cancer Society (ACS) 2006 Cancer Facts & Figures; Atlanta, Georgia

Projected by 2020: 10.3 Million Deaths and 16 Million New Cases

Global Cost of Cancer - $895 billion (L. Armstrong Foundation/ACS)

350 million smokers in China, 23% > over 65 by 2035

Source: IACR, WHO
# Reality of Metastatic Cancer

<table>
<thead>
<tr>
<th>Site</th>
<th>All stages</th>
<th>Local</th>
<th>Regional</th>
<th>Distant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast (female)</td>
<td>86.6</td>
<td>97.0</td>
<td>78.7</td>
<td>23.3</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>62.3</td>
<td>90.1</td>
<td>65.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Liver</td>
<td>6.9</td>
<td>16.3</td>
<td>6.0</td>
<td>1.9</td>
</tr>
<tr>
<td>Lung and bronchus</td>
<td>14.9</td>
<td>48.7</td>
<td>16.0</td>
<td>2.1</td>
</tr>
<tr>
<td>Melanoma</td>
<td>89.6</td>
<td>96.7</td>
<td>60.1</td>
<td>13.8</td>
</tr>
<tr>
<td>Ovary</td>
<td>53.0</td>
<td>94.7</td>
<td>72.0</td>
<td>30.7</td>
</tr>
<tr>
<td>Pancreas</td>
<td>4.4</td>
<td>16.6</td>
<td>6.8</td>
<td>1.6</td>
</tr>
<tr>
<td>Prostate</td>
<td>97.5</td>
<td>100.0</td>
<td>--</td>
<td>34.0</td>
</tr>
<tr>
<td>Testis</td>
<td>95.5</td>
<td>99.1</td>
<td>95.0</td>
<td>73.1</td>
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</tbody>
</table>
Reality of Today vs. the Vision That Is Extant for 21st Century Medicine

**Reality of Today**

- Healthcare spending in 2009 projected - $2.5 trillion
- Expected to rise one percentage point this year (17.9% of U.S. economy - largest increase since CMS began tracking)
- Increases expected to continue through 2018 ($4.4 trillion - ~20% of economy – 50% public spend)
- Investment in private healthcare declined (3.9% this to 15 year low; – prescription drug spending slowed (1.4%)

**21s Century Medicine**

- Focus on predisposition, early detection and biological processes
- Diagnosis based on molecular characterization of patients vs. morphologic and pathologic analysis
- Evidence-based - continually assesses standard of care –and rapidly integrates improvements
- Connects research with clinic in seamless feedback loop – using IT platforms

21st Century Medicine – Delivering Evidence Based Intervention at the Right Time for an Individual Patient
Driver for Innovation-Based Progress in Cancer Research – Ultimately Healthcare

Living in an Era of CONVERGENCE

MOLECULAR SCIENCES,
BIOINFORMATICS/COMPUTATIONAL SCIENCES,
PHYSICS, ENGINEERING

Defining Opportunity for Disruptive Innovation
# CSSI Programs Initiated to Enable Progress Toward Molecularly Based Cancer Medicine

## Focus/Need Area

<table>
<thead>
<tr>
<th>Focus/Need Area</th>
<th>NCI Initiative</th>
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</thead>
<tbody>
<tr>
<td>Physical Sciences</td>
<td>Physical Sciences Oncology Centers</td>
</tr>
<tr>
<td>Nanotechnology</td>
<td>Nanotechnology Alliance for Cancer</td>
</tr>
<tr>
<td>Cancer Genomics</td>
<td>Analysis – Functional Genomics Centers</td>
</tr>
<tr>
<td>Proteomics/Biomarkers</td>
<td>Clinical Proteomics Initiative</td>
</tr>
<tr>
<td>Large Scale Genomics</td>
<td>The Cancer Genome Atlas</td>
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<tr>
<td>Biospecimens</td>
<td>caHUB (Cancer Human Biobank)</td>
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</table>

## Bioinformatics: The Cancer Bioinformatics Grid – caBIG

*Note: Cost of these programs (without caBIG) ~2.7% of NCI’s total budget*
Examples of Fields/Programs Driving Innovation -

- Genomics – The Cancer Genome Atlas
- Physics/Engineering/Computation – Physical Sciences Oncology Centers Nanotechnology
- Nanotechnology Alliance
Biological significance of understanding genomic changes in cancer:

- Copy number
- Expression (regulation of)
- Regulation of translation
- Mutations
- Epigenome

Cancer is a disease of genomic alterations – identification of all genomic changes would enable defining cancer subtypes – potential to transform cancer drug discovery, diagnostics and prevention.
TCGA Network is Big Science

**Data Management, Bioinformatics, and Computational Analysis**
- Data Coordinating Center, DCC
- Analyses of data

**Genome Sequencing Centers**
- High throughput sequencing of genes and genomic regions identified through cancer characterization

**Cancer Genome Characterization Centers**
- Identification of expression alternation
- Detection of DNA fragment copy number changes and LOH
- Epigenetics

**Human Cancer Biospecimen Core Resource**
- Biospecimens-related data storage
- Histopathology confirmation performed
- Biomolecules isolated, QC’ed and distributed

**Technology Development**
- Increased sensitivity of molecular characterization platforms
- Analysis of biomolecules from 1000 cells or less

**Human Tumor Samples: DNA/RNA**
- Molecular Characterization Data
- Sequencing Data
- Analysis Approaches
TCGA: Glioblastoma Multiforme (Adult Brain Tumors) Subtypes Molecular Pathways

TCGA: Nature 2008
TCGA – Data Paralysis or Progress

DATA

DATA

DATA

DATA

DATA

Investigator Initiated Research

Drug Development

Molecular Diagnostics

Patients

Cancer Centers
Genomics Technologies – Closing in on the $1000 Genome

Source: Sequencing; IEEE Spectrum 2/10
Cancer: A Complex Information Driven Evolving System

- Inherited
- Chemicals
- Viruses
- Hormone
- Nutrition
- Sunlight
- Smoking
- Etc.

Fundamental Understanding of Cancer: Beyond Changes in the Genome, Need Knowledge of Changes in the “Biological Space”
Thinking Differently About Key Questions in Cancer

Including Innovation in the Equation
Innovation as Viewed by the NYT - Highlight from 2009

Grant System Leads Cancer Researchers to Play It Safe

“...One major impediment, scientists agree, is the grant system itself. It has become a sort of jobs program, a way to keep research laboratories going year after year with the understanding that the focus will be on small projects unlikely to take significant steps toward curing cancer...

...In fact, it has become lore among cancer researchers that some game-changing discoveries involved projects deemed too unlikely to succeed and were therefore denied federal grants, forcing researchers to struggle mightily to continue...

...the institute’s reviewers choose such projects because, with too little money to finance most proposals, they are timid about taking chances on ones that might not succeed...
Are We Doing Enough to Drive Disruptive Innovation?

- Rejects the most obvious solution to a problem – not just new answers – new questions
- Find ways to generate multiple “non-obvious” solutions
- Driven by individual insights At the “intersection” of fields/technologies
- Combines solutions and methods from unrelated fields
- Disruptive to current dogma – challenges assumptions
State of Biomedical/Cancer Research – the S Curve

- Data explosion
- Rise of Partial Theories of complex systems
- Growing Realization of Of Subsystems
- Larger Scale – Data Standards
  - Data explosion
  - Reductionist-Driven Studies - Duplication
- Search for Unifying Theories
- Point of Convergence of the Biological And physical Sciences
- TCGA

Adapted from E. Zerhouni

From Qualitative to Quantitative
Complexity: No two snowflakes are alike

Micro (heterogeneity) vs. Macro (problem)
Complexity: Copy Number Alterations in GBM and Ovarian Cancers
Convergence Across the Genome = Data
“Tsunami” = May be Paralyzing Complexity

It’s single gene changes
It’s Pathways
It’s Proteins
It’s the Chromosomes
It’s Epigenomics
Cancer is a Result of Translation of Digital Information Across Length and Time Scales

For decades, we have endeavored to deconvolute the complexity of cancer by understanding each part at its most basic level. However, it is the interactions (across scales) that lead to emergent properties of cancer.
Investigators tend to work in single ‘length-scale’. A real understanding of cancer will require working across scales.
Building an Innovation Driven System of 21st Century Cancer Medicine – All Medicine
Innovation: Create a Personalized Cancer Medicine System

- Connected and interoperable IT infrastructure to translate research advances
- National system of biospecimen collection – storage – characterization, stewardship and access
- Technology standards
- Compendium of all genomic changes in all tumors/ subtypes
- Defined/validated biomarkers – signatures – as appropriate for all tumors/subtypes
- Appropriate and Responsive translational research infrastructure
- New clinical trials models – and networks
- Payer inclusion in process – enable reimbursement through involvement and knowledge