The IMAT Program

Reflections on 15 years of progress and opportunities for the future

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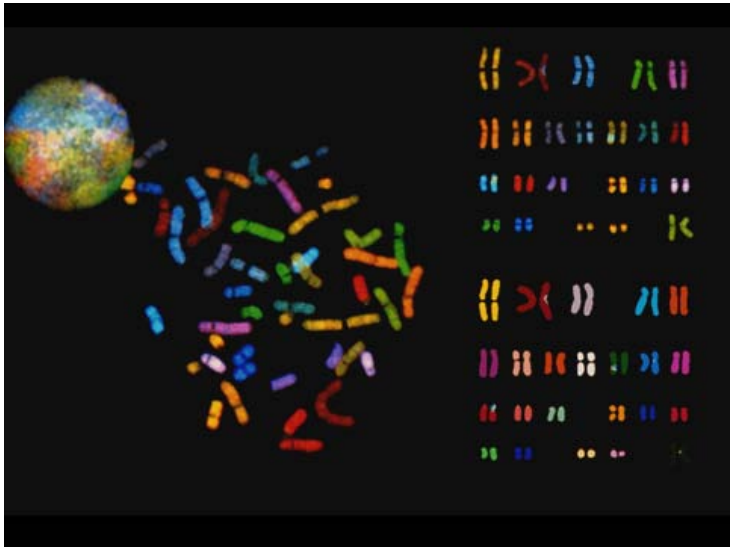
Executive Director
The Lemelson Foundation
improving lives through invention

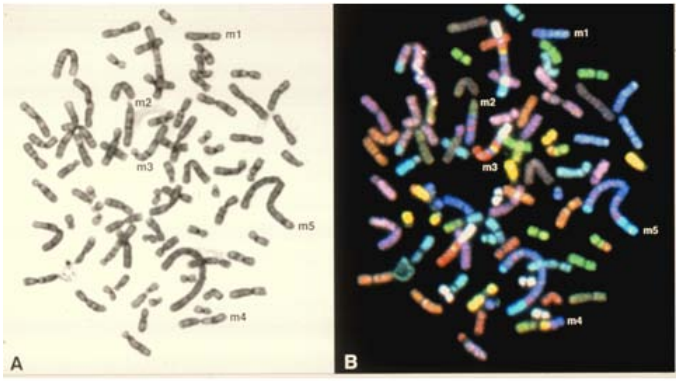
November 2011

NCI: Dedicated to Discovery

Key Questions About Cancer

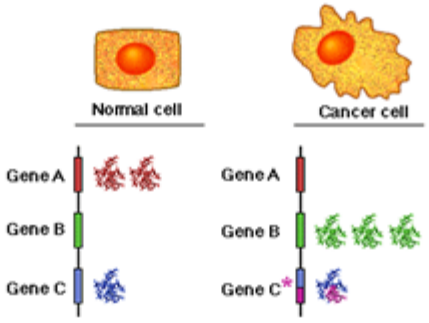
- Nature of Cancer: What is cancer and how does it develop?
- Cancer Risk: Who is at risk and why?
- Prevention: How can cancer be prevented?
- Detection: How do we screen for, detect, and diagnose cancer?
- Treatment: How is a given cancer best treated?
- Rehabilitation: How might the quality of life for cancer patients and survivors be improved?





The Genetic Basis of Cancer

- Cancer results from the gradual accumulation of multiple genetic changes in single cells



Where Did the Vision Begin?

Genomic Approach

- Assess the contribution of any gene or gene product, from the complete catalogue of genes and gene products, to defining a particular biological or pathological state
- Requirements
  - Information infrastructure
  - Cost-effective, comprehensive analysis technologies

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Pathway to Technological Success

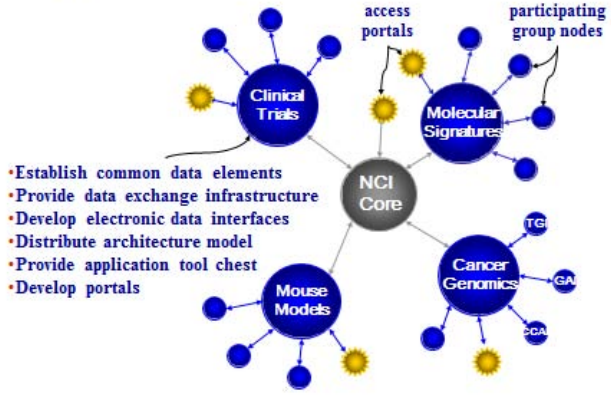
- Automation
- Parallelism
- Miniaturization

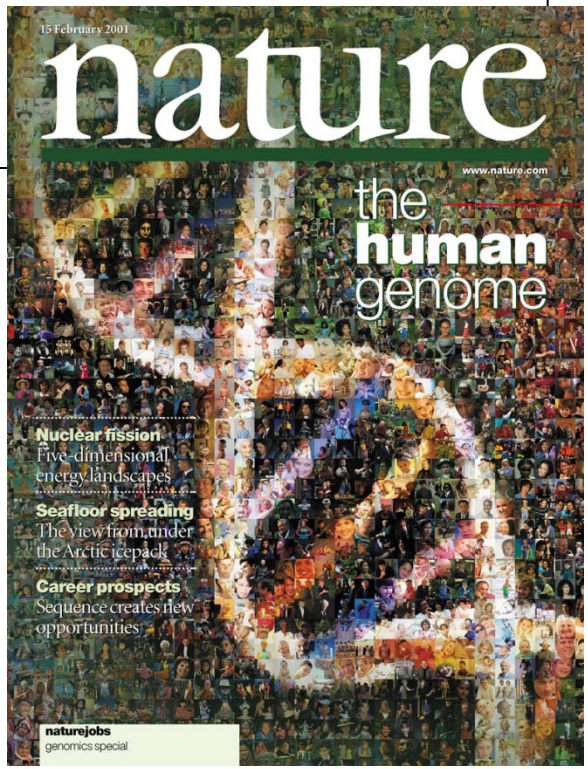
Types of Efforts

- Who
  - Non-profit
  - Industry
- Goal
  - Research
  - Instrumentation
  - Service
- Target Market
  - Research
  - Diagnostics
  - Genomics

NCI Center for Bioinformatics

building common architecture, common tools, and common standards





Innovative Molecular Analysis Technologies Program

Creating the Toolkit to Enable Molecular Discovery and Speed Cancer Research

Technologies suitable for in vitro, in situ, in vivo, and in silico analysis of:

- –alterations and instabilities in genomic DNA
- –expression of genes and gene products
- –cellular localization, post-translational modification, and function of proteins; and
- –monitoring major signal transduction networks involved in cancer

Matching the Goals with the Tools

- *Sought new contributors*
- *Urged multidisciplinary approaches*
- *Fostered collaboration*
- *Consolidated articulation of NCI's needs*
- *Milestone based performance review*
- *Special Review*
- *Engaged Industry*
- *Expected technology maturation plans*

Phased Innovation Award

- Created to support technology research from the evolution of innovative concepts through feasibility testing, to subsequent full-scale development
- Single submission and evaluation of both the R21 and the R33 as one application, including:
  - R21 phase - including measurable milestones
  - R33 phase - including a credible development plan

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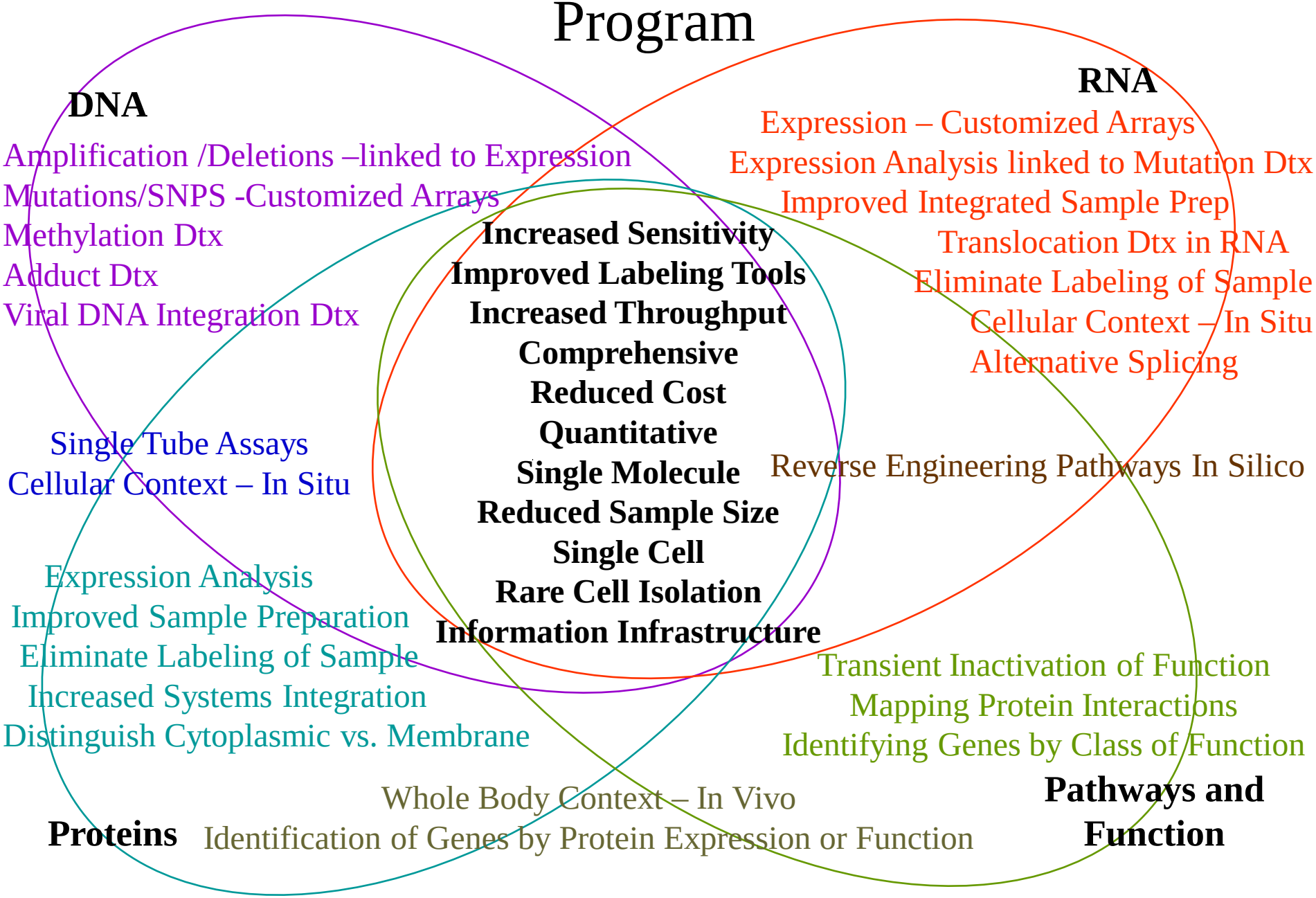
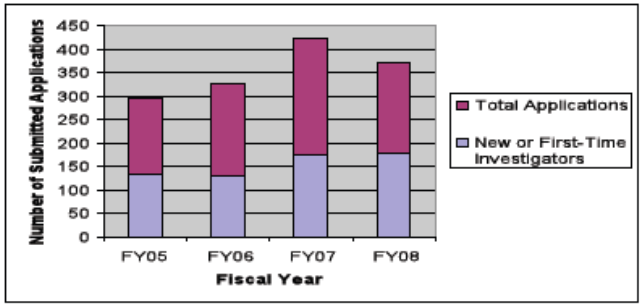
Innovative Molecular Analysis Technologies Program



Measuring the Program Impact

IMAT Impact: New, First-Time, or Early Career Investigators



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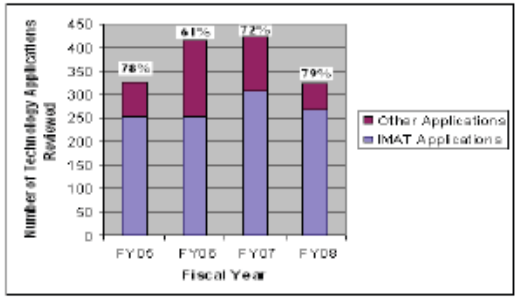
IMAT Contributions to the NCI Technology Development Portfolio (FY 2005-2008)

IMAT Contributions to the NCI's Technology Development Portfolio as a Function of All Technology Applications Reviewed by the National Cancer Institute



Source: 2008 Annual Report of the NCI Division of Extramural Activities

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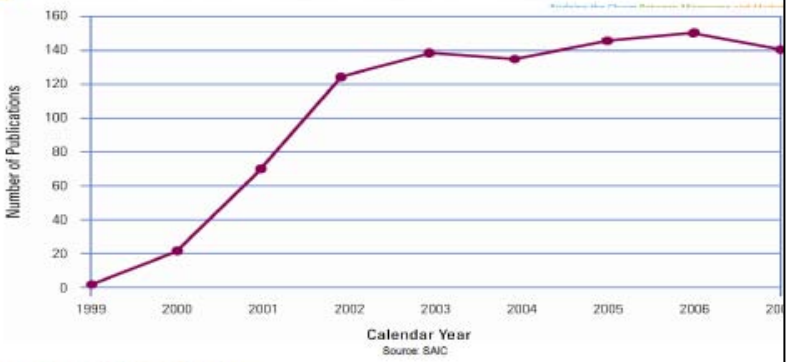
IMAT Impact: Number of Articles in Peer-Reviewed Journals Citing IMAT Grants Through 2007



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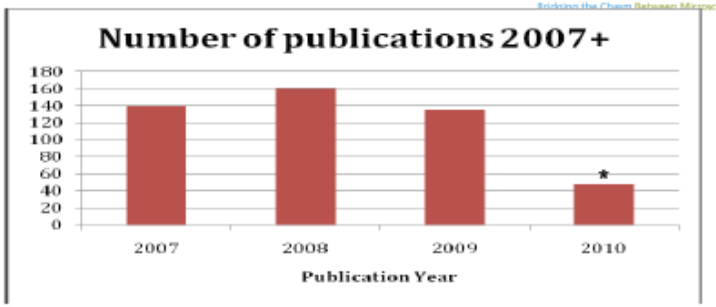
IMAT Impact: Publications Between 2007 and May, 2010 That Specifically Cite IMAT Awards



* Through the first 5 months of 2010 (i.e. May, 2010)

2008 – 2010 Publications include: 12 Nature publications, 7 Proceedings of Nat'l Academy of Sciences publications, and 3 Cell publications

Source: Science and Technology Policy Institute, Washington D.C.

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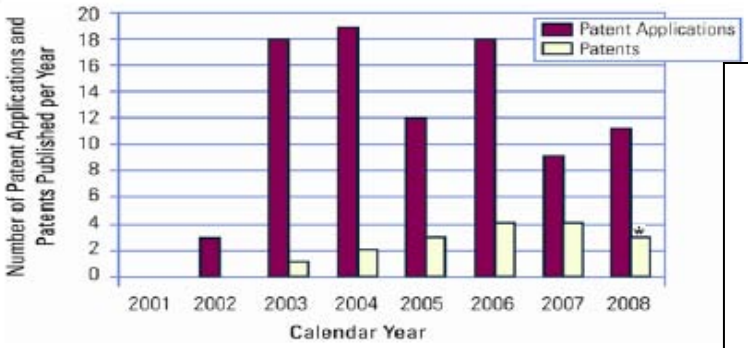
Translating Inventions to Tools

IMAT Impact: Number of Patent Applications Filed and Received That Specifically Cite An IMAT-Related Award (Source: USPTO)



*As of August, 2008

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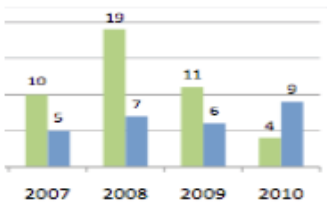
IMAT Impact: Number of Patents and Patent Applications Citing an IMAT Award Between 2008 and May, 2010

Bridging the Chasm Between Microscope and Marketplace



Year of publication (for applications) and year of patent receipt (for patents)

Applications Patents

71 new patent submissions, 27 USPTO *approved* patents in 2.5 years!

Source: Science and Technology Policy Institute, Washington DC and USPTO

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IMAT Impact: Invention Count and Institutions Represented

Bridging the Chasm Between Microscope and Marketplace

Grantee Name
ALLEGHENY-SINGER RESEARCH INSTITUTE
AMBION, INC
BAYLOR COLLEGE OF MEDICINE
BRIGHAM AND WOMEN'S HOSPITAL
CHILDREN'S HOSPITAL OF PHILADELPHIA
COLD SPRING HARBOR LABORATORY
COLUMBIA UNIV NEW YORK MORNINGSIDE
GEORGIA STATE UNIVERSITY
HARVARD UNIVERSITY
ILLUMINA, INC
INSTITUTE FOR SYSTEMS BIOLOGY
INTRONN, LLC
JOHNS HOPKINS UNIVERSITY
MASSACHUSETTS GENERAL HOSPITAL
MASSACHUSETTS INSTITUTE OF TECHNOLOGY
MEDICAL UNIVERSITY OF SOUTH CAROLINA
NORTHWESTERN UNIVERSITY
ROCKEFELLER UNIVERSITY
SIDNEY KIMMEL CANCER CENTER
STANFORD UNIVERSITY
TUFTS UNIVERSITY BOSTON
UNIVERSITY OF ARKANSAS MED SCIS LTL ROCK
UNIVERSITY OF CALIFORNIA
UNIVERSITY OF CALIFORNIA BERKELEY
UNIVERSITY OF MARYLAND COLLEGE PK CAMPUS
UNIVERSITY OF MISSOURI
UNIVERSITY OF TEXAS MD ANDERSON CAN CTR
UNIVERSITY OF TEXAS SW MED CTR/DALLAS
UNIVERSITY OF WASHINGTON
UNIVERSITY OF WISCONSIN MADISON
VANDERBILT UNIVERSITY
WISTAR INSTITUTE OF ANATOMY AND BIOLOGY

172 Inventions with patents / patent applications based on IMAT grant awards! And counting!

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Has IMAT Achieved It's Goals?

IMAT "Blockbusters": Example 7
ICAT

Partnering for Cures | A RoseCures Meeting

Bridging the Chasm Between Microscope and Marketplace

Rudolf Aebersold, Ph.D. , *Institute for Systems Biology*

- IMAT Award: Isotope Coded Affinity Tags (ICAT) for Quantitative Proteomics (2000)
- Impact: Large-scale analysis of complex samples, including whole proteomes and small-scale analysis of subproteomes; 218 publications in Pubmed on ICAT technology, 34 focusing on cancer.
- 7 patent applications filed or already granted (Methods for Isolation and Labeling of Sample Molecules, Patent 7,183,116)
- Patents Filed or Granted: Methods for Isolating and Labeling Sample Molecules (20020168644, 20040265810, and 20040110186), Methods for High Throughput and Quantitative Proteome Analysis (20040033625), two with the title Methods for Rapid and Quantitative Proteome Analysis (20020119490 and 20060008851) and Androgen-Regulated Genes and Uses for Diagnosis, Prognosis and Treatment of Prostate Neoplastic Conditions (20040121413).

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IMAT "Blockbusters": Example 2
RNA Later and Derivatives

Partnering for Cures | A RoseCures Meeting

Bridging the Chasm Between Microscope and Marketplace

Gary Latham, Ph.D., *Ambion, Inc.*

- IMAT Award: Enzymatic Tools for Degrading Tissue and Preserving RNA *(2001); SBIR Phase II Awardee (2005-2007)*
- Impact: Researchers can store tissue samples without significant loss of RNA integrity
- Patented (application serial number 60/514,313)
- Commercially released by Ambion in February, 2005

Schematic of RNAlater™ Procedure.

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MGA Technology
ALA 2008 "Innovation of the Year"

Partnering for Cures | A RoseCures Meeting

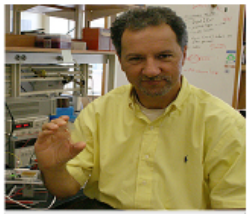
U.Va. professor receives Innovation Award from the Association for Laboratory Automation

Posted 02/07/08

James Landers, professor of chemistry and mechanical engineering, and associate professor of pathology, was recently recognized with the 2008 Innovation Award from the Association for Laboratory Automation (ALA) for his novel Microfluidic Genetic Analysis (MGA) technology.

The ALA presented Landers with this honor, which includes a $10,000 prize, at LabAutomation2008 in Palm Springs on January 30. This highly competitive award is made annually at the LabAutomation conference for "exceedingly innovative" work that contributes to research on automated technologies in the laboratory.

ALA Innovation Award Chairman William Sonnefeld, Ph.D., said the competition was extremely strong and he was very pleased with the variety and quality of submissions for this year's award, but Landers' presentation was a standout. "All of the presentations were fantastic but Doctor Landers' presentation edged out the other finalists. It was a tough competition but the panel felt that his presentation in particular deserved the award," said Sonnefeld. "The ALA Innovation Award was created to recognize this type of leading-edge work and the outstanding scientist behind it."



James Landers
Photo by Melissa Mahr

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BIG NEWS IN SMALL TECH.

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small tech 2001

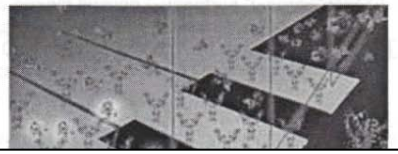
life sciences

RESEARCHERS FIND EFFICIENT WAY OF TESTING FOR PROSTATE CANCER

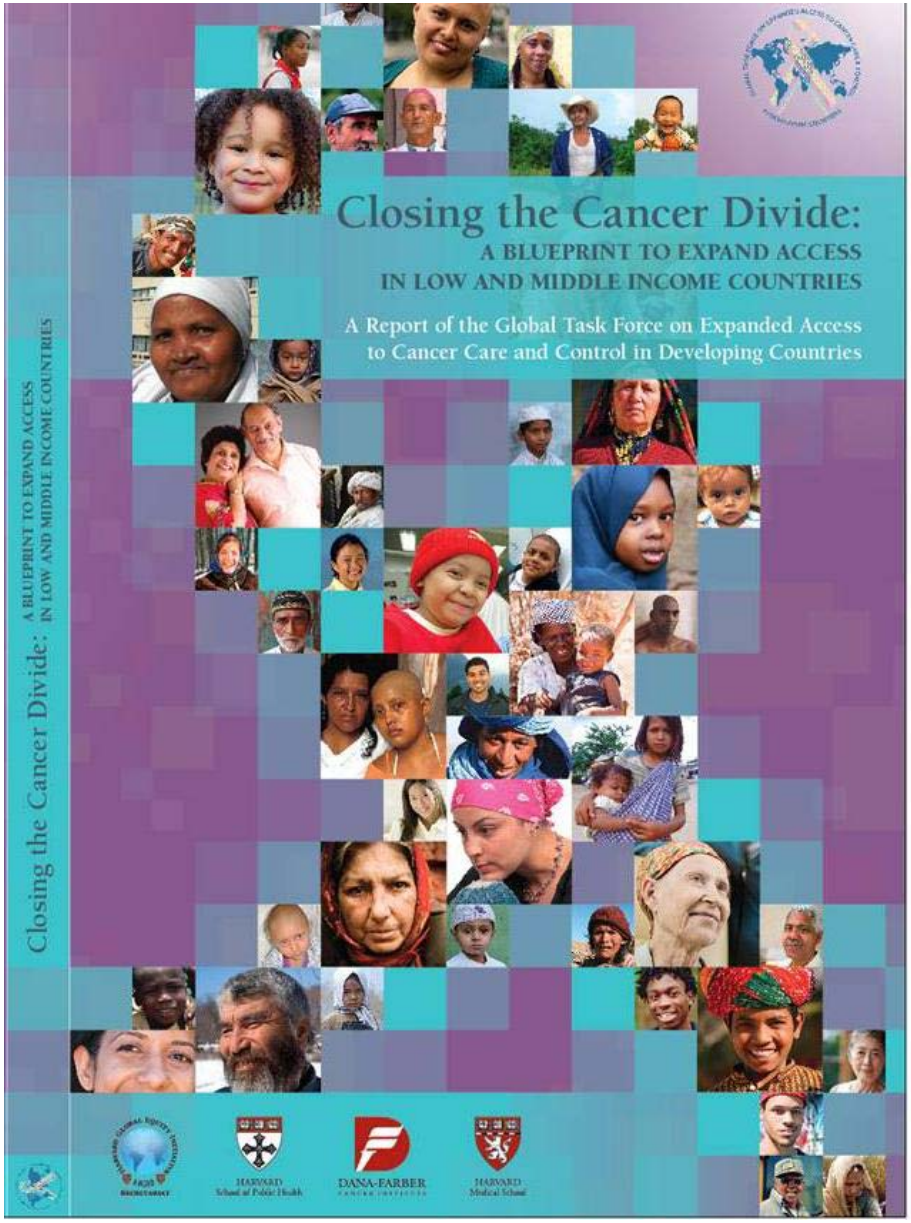
By Rosemary Clandos
Small Times Correspondent

Sept. 4, 2001 -- A team of researchers has developed a sensor that uses microscopic "diving boards" – a technological development that could cut the cost of detecting prostate cancer.

Arun Majumdar, a professor of mechanical engineering at the University of California, Berkeley, published his findings Saturday in the journal Nature Biotechnology. The technique brings together tiny cantilevers -- developed in the past few years to detect DNA and other chemicals -- and protein chips, which are being commercially produced for analysis of DNA and RNA.



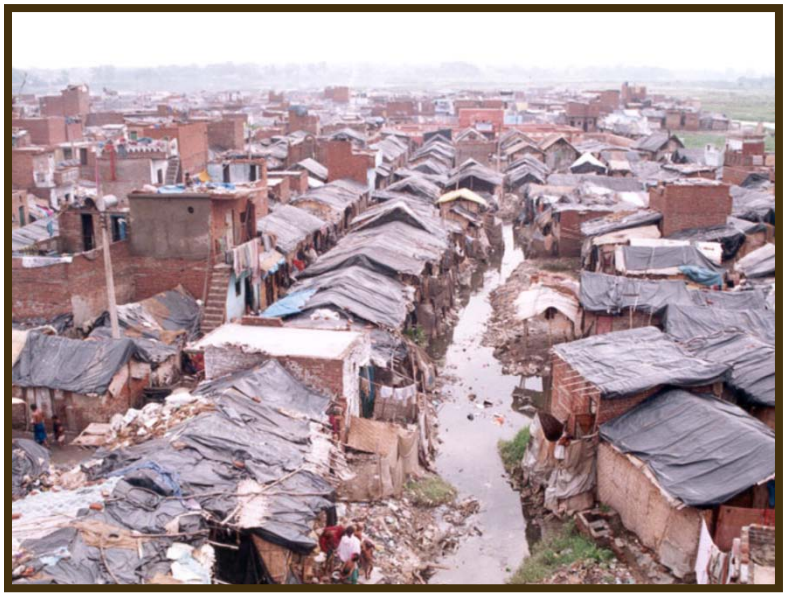
Expanding Global Focus



RECOMMENDATIONS

1. Efforts to reduce the risks for cancer and other NCDs posed by tobacco use, inactivity, and unhealthy eating should be incorporated into anti-poverty and social welfare programs.
2. Many existing health system platforms and programs could incorporate elements of CCC. Programs for reproductive, maternal and child health, social welfare, and anti-poverty are examples. Specific opportunities need to be identified, and then interventions developed, and evaluated.
3. Non-specialized health care workers should be trained to diagnose and provide core treatment, where appropriate and especially for the candidate cancers identified in Section 5, and in areas and communities where no specialized cancer care is available. This does not substitute for trained oncologists and specialists, but can make their services more accessible to many.
4. The use of communications technology and telemedicine should be expanded to provide access to diagnosis and specialized care in remote areas through partnerships and linkages with distant oncology specialists. This technology also should be used to share diagnostic information, data and knowledge, and for training and continuing education.
5. Tertiary treatment centers, cancer institutes, and bilateral donors should consider establishing dedicated funds to support the expansion and solidification of existing pilot programs and to establish new initiatives.
6. Alternative innovative and complimentary delivery mechanisms should also be identified, evaluated, and scaled up to close the gap between need and available resource capacity.
7. Lessons learned from innovative CCC programs and experiences should be adapted and incorporated into large-scale programs to increase access, improve quality, and bring care closer to home and community.
8. A data base of existing CCC programs, technologies, and lessons learned needs to be developed, financed, and institutionalized to make the evidence easily accessible for translation into policy and programming. Results should be shared globally through a clearinghouse of information that could be based at WHO or IARC.

The Context



- 6.8 B people live in the world
- 1.4B live on less than $1.25 per day; 70% of those people live in rural settings
- 98% of the world's undernourished live in developing countries (952M)
- 2.5 B lack sanitation and 982 M lack access to clean water
- of children in developing countries are undernourished; malnutrition contributes to over 1/3 of child deaths
- 34M people living with AIDS and 12M people living with TB
- 99% of newborn deaths (~4M) and pregnancy-related deaths (>0.5M) in women in developing countries

Health Solutions for the Poorest

Creating health solutions appropriate for the most resource poor settings on earth

What challenges exist?

- **Basic science has been underserved**
- **Appropriate technologies are missing**
- **Little appeal for industry**
- **Regulatory path forward is complex or nonexistent**
- **Sustainable solutions need local ownership**

Basic Science has been Underserved

- **The poorest populations have ongoing issues with malnutrition and concurrent infections**
- **Basic understanding of the relationship between malnutrition, concurrent infections, and immune status contributing to state of health and ability to respond to therapy is lacking**
- **Understanding the role of microbiome in nutritional and immune status and resulting response to intervention is needed**

Solutions require integrating across complex systems and disease states; silos wont get us there.

Additional resources should be targeted to the worlds biggest problems

Appropriate Technologies are Missing

- **Large numbers of those we hope to reach currently don't have effective access to health systems infrastructure (~50% of people in sub-Saharan Africa)**
- **For those settings it should be assumed that there is no clean water, non-existant or intermittent electricity, and care providers with minimal to no health services training**
- **Social and cultural issues can limit options for solutions**
- **Neglected ethical considerations can bring research to a halt**

Greater attention should be paid to defining the target product profiles needed for the worlds most resource poor settings.

Technologies can not be driven solely by northern perspectives

Technology development requires considering the ethical, social and cultural framework of those that are targeted

Industry has not Fully Engaged

- **Market opportunities are not apparent**
- **Market opportunities frequently don't match northern expectations of return on investment, yet may support entirely viable local businesses**
- **Target product profiles are unclear**
- **Partners with development experience relevant to the targeted setting may not be apparent**
- **Regulatory ambiguities and complexities are a deterrent**
- **Public health community can be resistant to industry involvement**

The reality of the market opportunities need to be defined

Partners with relevant domain and development expertise in the targeted geographies and populations need to be available and visible

New business models need to be explored and supported

Public health community needs to embrace the reality of the contribution of the private sector to health solutions that reach communities and have impact

Regulatory Path Forward is Complex

- **Every country has a different process; the complexity of addressing so many countries (ie continent of Africa) with diverse and uncharted pathways is daunting**
- **Some countries are lacking expertise and a coherent process**
- **In some countries the bulk of services are delivered through unregulated private providers**

The critical path for new technologies and health solutions need to be mapped early so that weak points in the regulatory path can be identified

Creativity and persistence is needed in engaging thought leaders and regulators early to define pathways where the path is unclear or to adapt existing processes to the benefit of new solutions.

Sustainable Solutions need Local Ownership

- **Parachuting in northern solutions almost never works for the long haul**
- **Ethical, social and cultural issues influence likelihood of uptake and therefore impact**
- **Northern investigators have been historically poor in engaging in equal partnerships and appropriately valuing the scientific contributions of local scientific partners**

Local scientist and thought leader involvement speeds acceptance

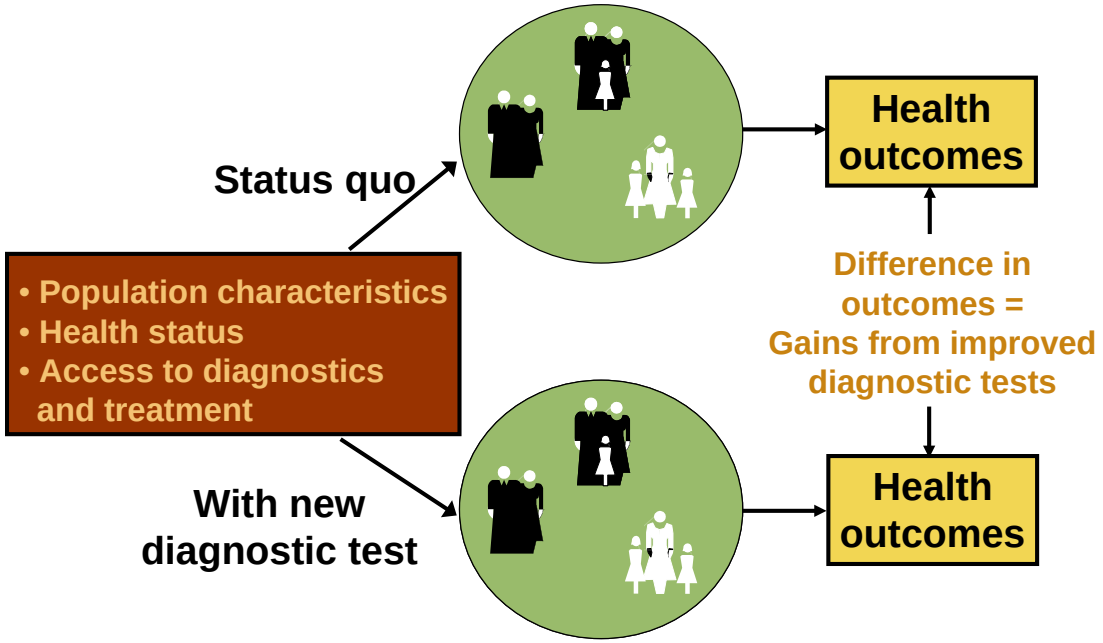
Local community engagement must be considered in both research and delivery

Local innovations may better match the needs of the community and therefore have a greater likelihood for sustained impact

It is local leaders that shape regulatory and policy change

Outputs from the Diagnostics Forum

1) ***The need to increase access to existing diagnostics***
2) ***Development & validation of new diagnostic tools from existing or emerging platforms***
3) ***Discovery and validation of new diagnostic markers***
4) ***Development of new diagnostic platforms to meet access needs, and the need to diagnose multiple diseases with common presentation***



Levels of Infrastructure Available

Advanced/Moderate

- Hospitals and urban clinics
- Electricity, clean water, well–equipped laboratories, trained clinicians

Minimal

- Health clinics (Africa), rural clinics (Asia, Latin America)
- No reliable electricity or clean water, no laboratory, minimal expertise

None

- Village or community
- No electricity, clean water, physical infrastructure, or trained staff

DX Platforms for Global Health

Requirements for resource poor settings

- Portable, limited logistics, no medical waste, self contained or no power, no water
- Capable of handling multiple specimen types
- Capable of multiplexed testing - DNA, Proteins, RNA, Metabolites
- Nearly fully automated operation (including sample prep)
- Low requirements for user training
- Extremely low cost of ownership

Needs for Technology Innovation

Sample Collection

- **design platform to accommodate new modes of sample collection**

Pre-Processing

- **need portable methods**

Detection

Sensitivity

- need performance adequate to inform decision making

Selectivity

- need receptors and/or reactions that are selective and robust

Displaying Results

- **need simple, unambiguous displays**

Waste Disposal

- **need built in waste management**

Questions to Ask

- **Is it the right product?**
  - Can it work in that setting? For that population?
  - Is it something the user would want?
- **Could it reach those in need?**
  - Can the innovation be accessed?
  - Is there a regulatory path to acceptance?
- **What type of partner can help to get it to those in need?**
  - Public sector
  - Private sector
  - Local solutions for local problems

An Enormous Opportunity for Impact Exists

How will the Opportunity be Realized?

- **Focus on the goal; define the problem in context**
  - **Engage the end user; focus on the patient**
  - **Consider and embrace social, ethical and cultural issues**
  - **Recognize the complexity**
- **Stimulate innovation**
  - **Engage global intellect**
  - **Right size the investments**
  - **Leap frog barriers**
- **Focus on sustainability**
  - **Understand the value proposition**
  - **Partner with others who have experience**

Thank you