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Accelerating Success through Strategic Innovation

Innovation Opportunities from Technology Convergence

Observations from Technology Cross-over Activity in the Boston and Cambridge Biotech Community

BioTech 2005 Conference
Enterprise Development Corporation
and University of Miami, Florida

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EDC BioTech 2005 PG

Outline

- Observed Convergence Paths
- Nano-Fluidics Convergence Example
- Molecular Imaging Convergence Example
- Clinically Driven Convergence Example
- Questions and Discussion

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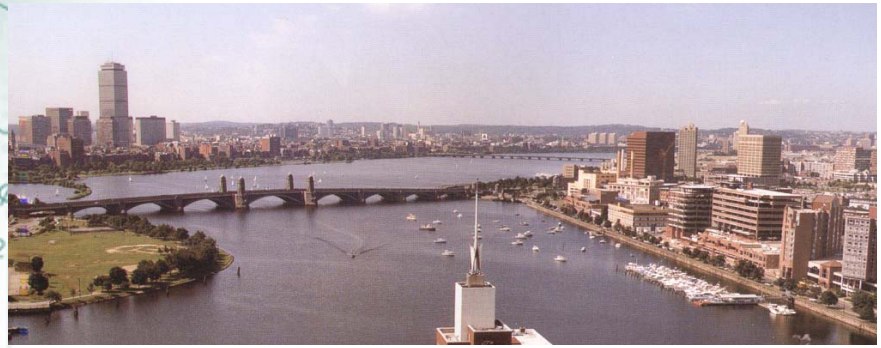
Spun out of the MIT Innovation Center in 1986, with offices in Cambridge, Massachusetts, Product Genesis has helped clients successfully and strategically innovate for over 18 years.



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What Is Strategic Innovation?

innovation n.

1) The action of innovating; the introduction of novelties; the alteration of what is established by the introduction of new elements or forms.
2) A change made in the nature or fashion of anything; anything newly introduced.

Oxford English Dictionary

Strategic Innovation n.

1) Change that has meaningful business consequences; new product concepts that add directly to the bottom line.
2) New ideas that fundamentally change the basis of competition within an industry.

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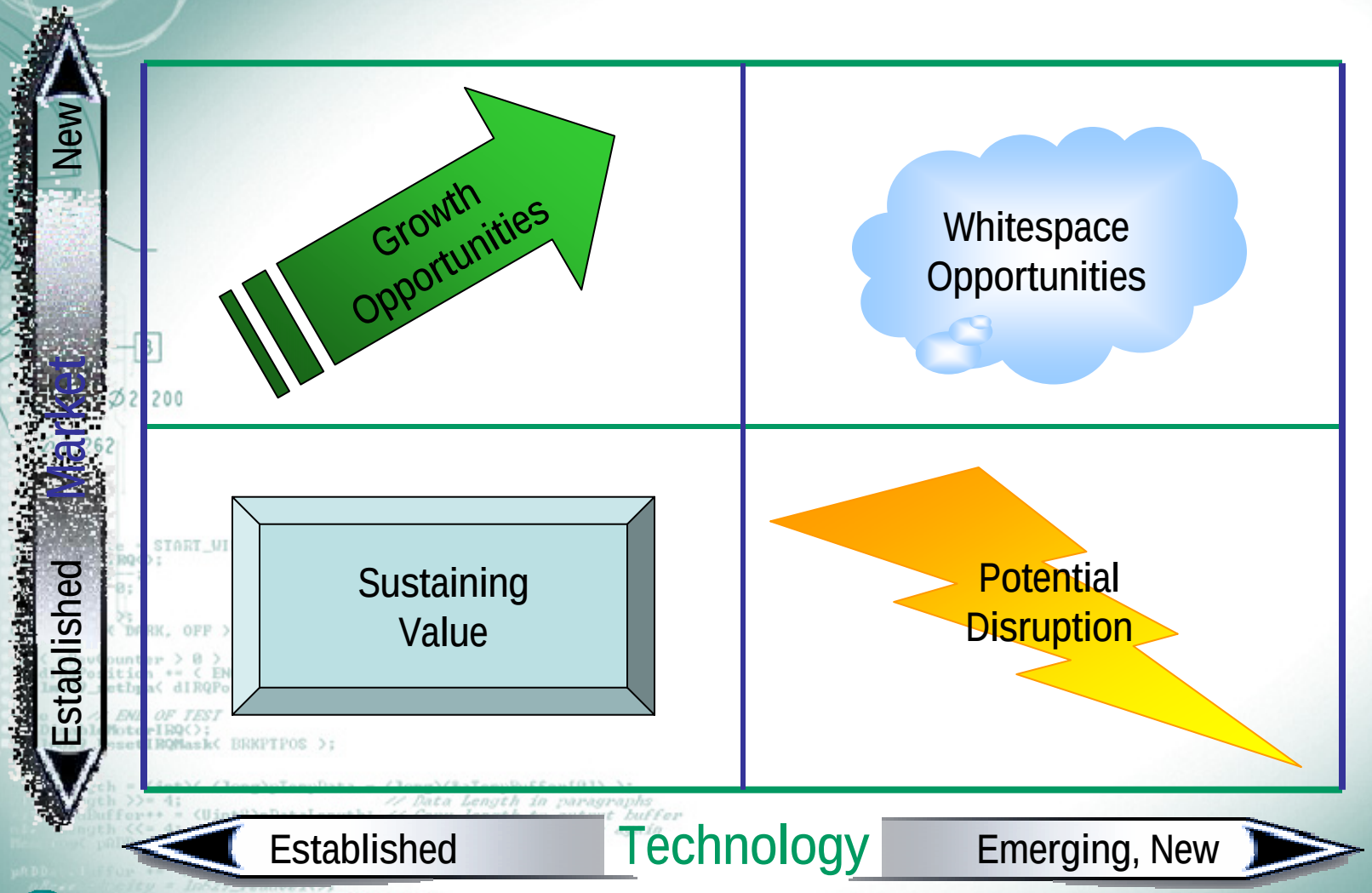
Strategic Innovation Opportunity Space



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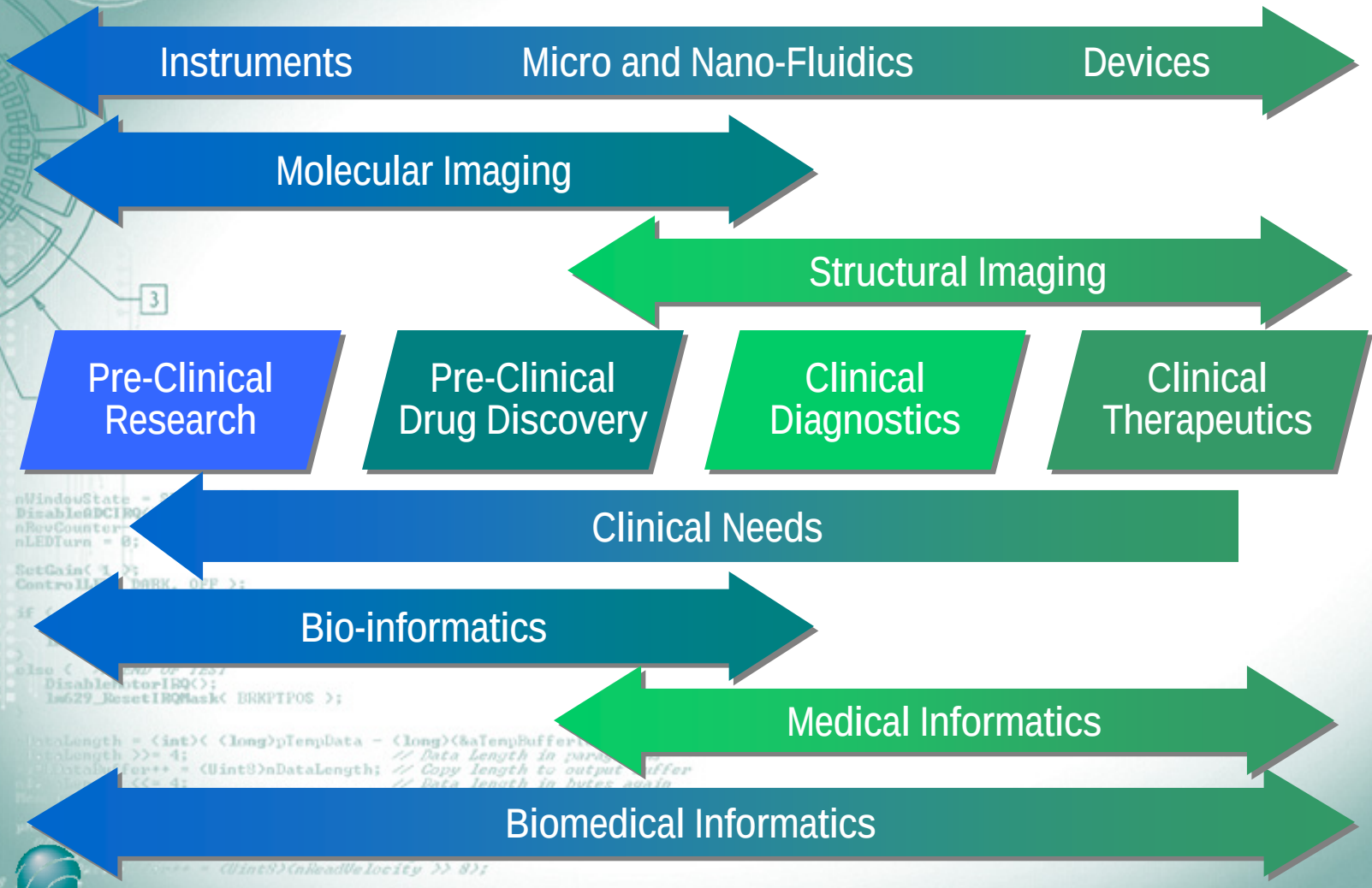
Parallel Technology Paths that Support Biotechnology Innovation



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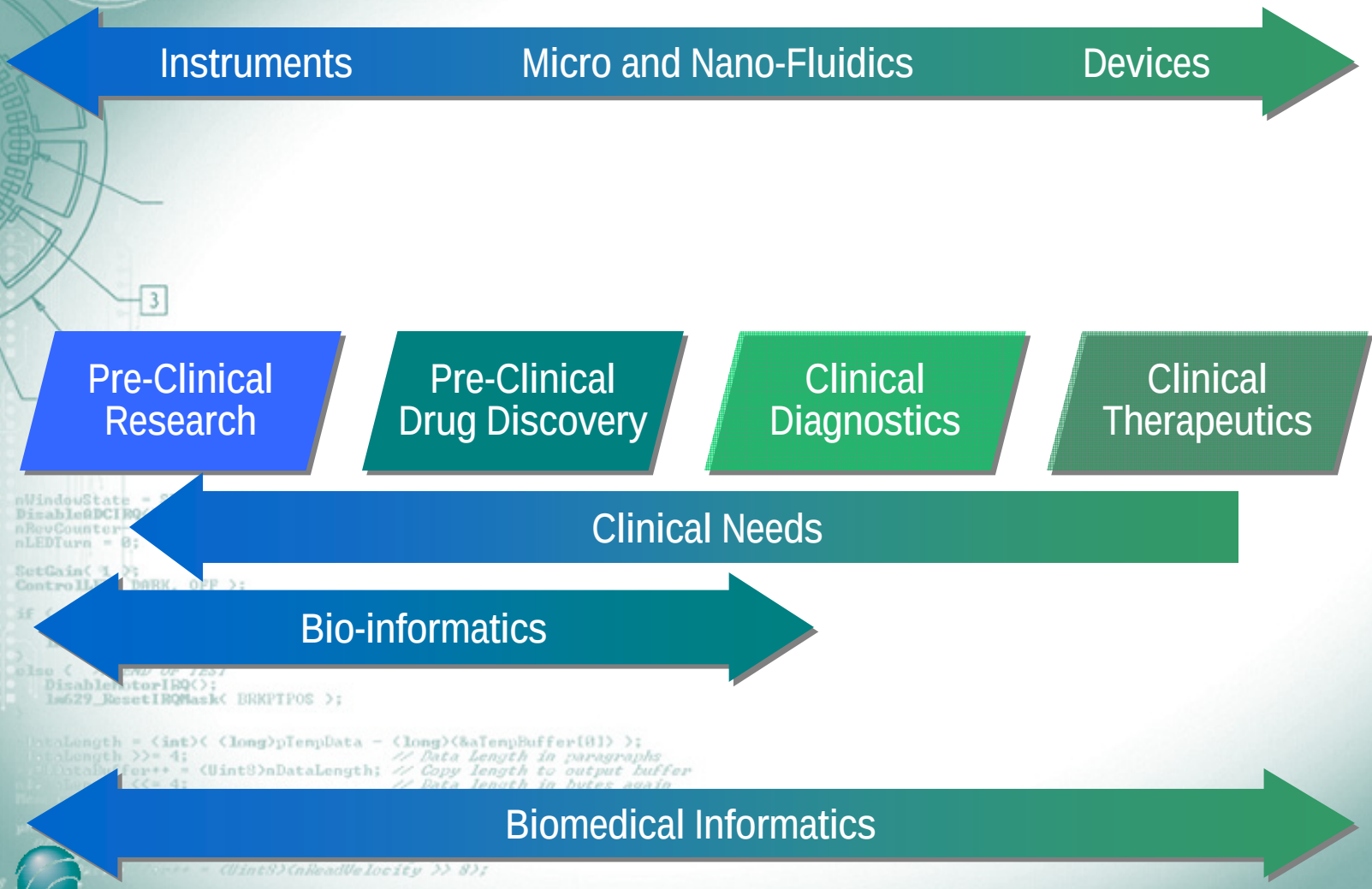
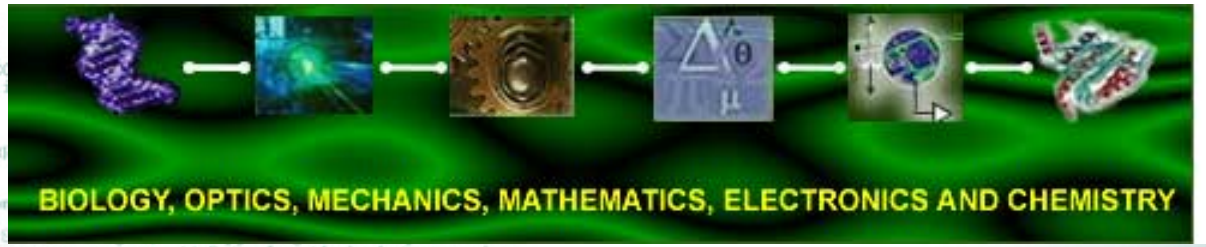
Nano-Fluidics Convergence Example



Innovation Source: Bioinstrumentation Laboratory at MIT

- Multi-disciplinary laboratory headed by Prof. Ian Hunter
- All researchers must be fluent in at least two disciplines:
  - Biology, Chemistry, or Biotechnology AND
  - Mechanics, Electronics, Optics, Mathematics, or Information Technology
- Groundbreaking work in nanotechnology applications for biotechnology and drug delivery



Innovation Results:
BioTrove – OpenArray and LivingChip

- Massively Parallel Nano-Array Systems
  - Over 25,000 Array elements per Slide
  - Compatible with Conventional Micro-plate Readers
- Convergence of Mechanical/Fluidics with Biotech Applications
  - Elegant Simplicity of Architecture
  - Utilizes Basic Material Properties paired with Basic Fluidics Properties
- Convergence of Informatics with Molecular Libraries
  - Libraries of Bio-informatics Data
  - Libraries of Molecules in Chips

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Innovation Results:
BioTrove – Massively Parallel Antibody Phase Screening

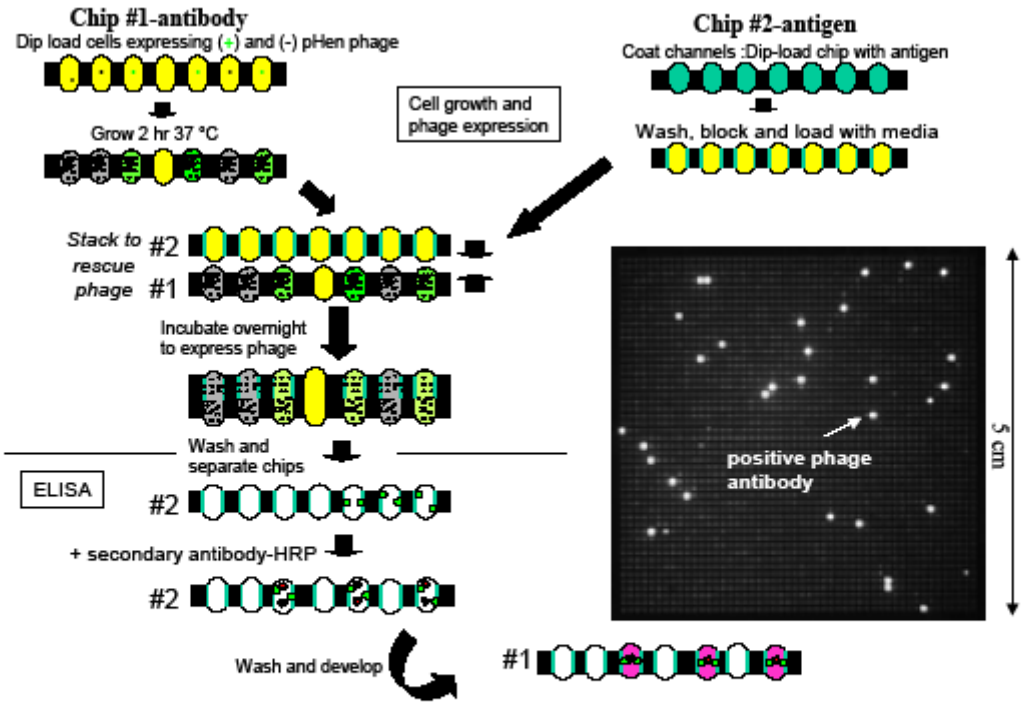

Figure 7: Outline of protocol for antibody phage library screening including the ELISA assay steps. An antibody library was dip-loaded into one 10,000-channel chip, cultured for two hours and then stacked with a 10,000-channel antigen chip. The stacked arrays were incubated, washed and separated and the antigen chip developed with a standard ELISA protocol to generate fluorescent signal in channels where there was a high affinity antibody-antigen complex.

Innovation Commercialization

- BioTrove has successfully closed over $20 million in financing
- Major pharmaceutical partners for Drug Discovery
  - Pfizer
  - Others (undisclosed)
- Commercially available OpenArray Systems
  - SNP Genotyping
  - qPCR Transcript Analysis
  - Pathogen Detection
  - ELISA Testing
- Broad Intellectual Property Portfolio
  - Core Patents licensed from MIT
  - Conflicting Patents acquired from Genecor
  - Application Patents licensed from Stanford

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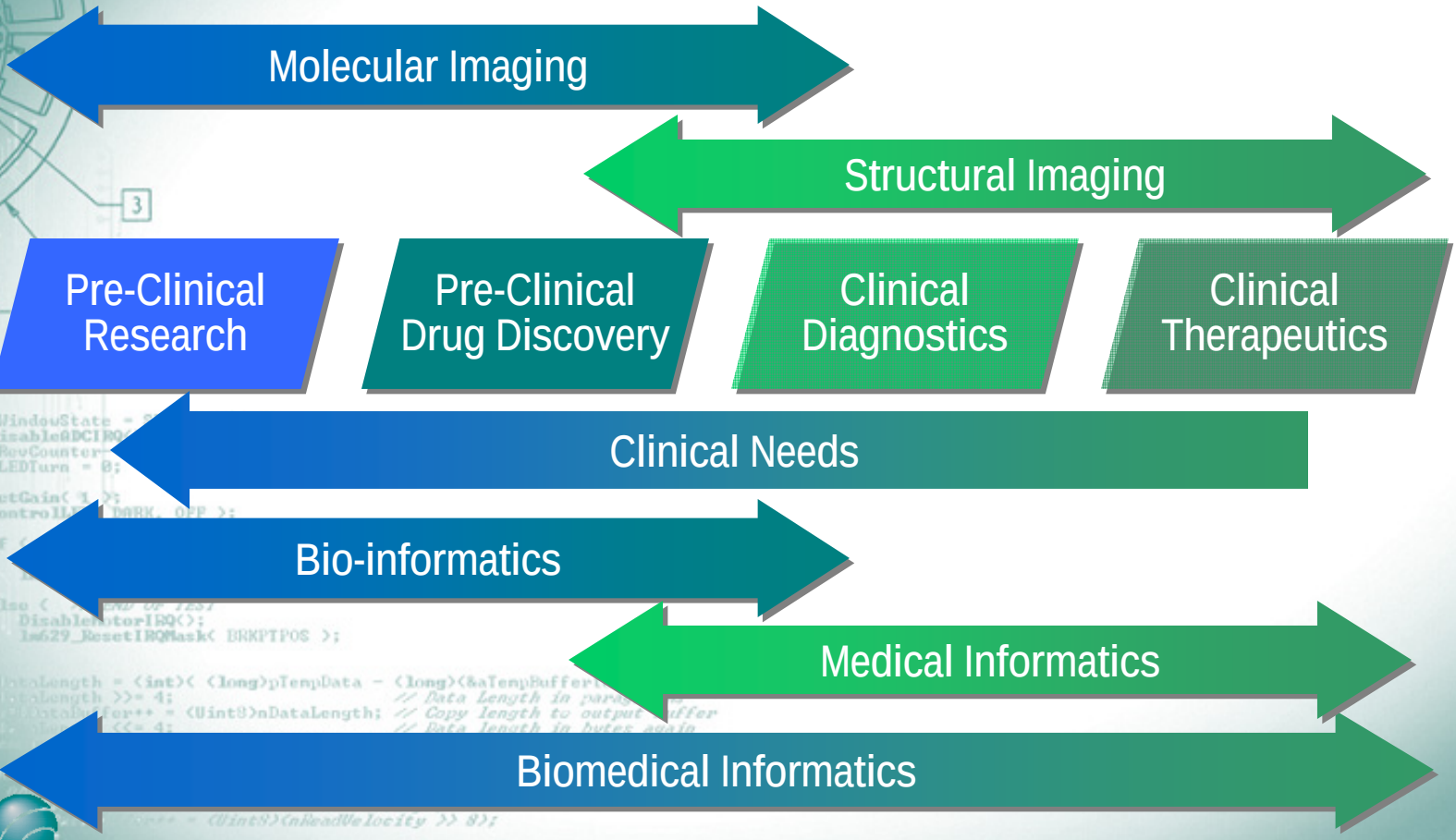
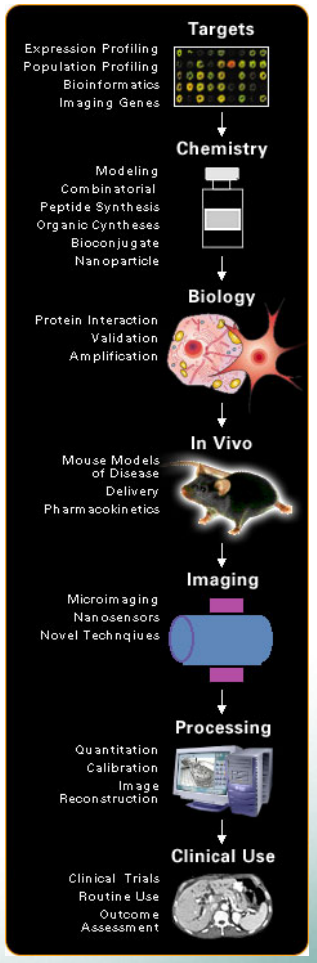
Molecular Imaging Convergence Example



Innovation Source:
Center for Molecular Imaging
Massachusetts General Hospital, Harvard Medical School

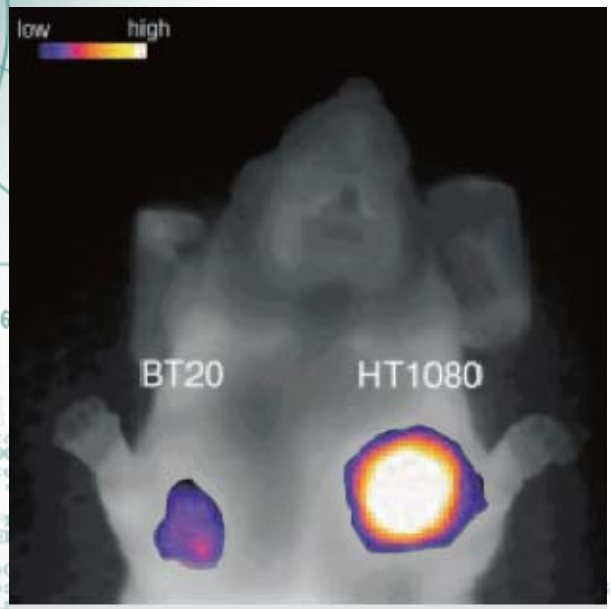
- Multi-disciplinary laboratory headed by Dr. Ralph Weissleder, MD, PhD
- Cross-disciplinary team covering:
  - Molecular Biology
  - Cell Biology
  - Biochemistry
  - Bio-informatics
  - Radiology
  - Cardiology
  - Oncology
  - Immunology
- World-leading research in the molecular phenomena of disease.
- Ultimate target, *in vivo* sensing and imaging of molecular level events.



Innovation Results: MGH/VisEn/SIEMENS – Fluorescent Molecular Tomography

- *In Vivo* 3D imaging of Biochemically Active Sites
  - Mouse Animal Model
  - Oncology and Atherosclerosis Targets
  - Pharmacological Activity Verification
- Convergence of Biochemistry with Optical Engineering and Image Processing with Biotech Applications
  - Exceptional specificity
  - Tomographic Image Reconstruction
- Convergence of Structural Imaging with Molecular Diagnostics and Imaging
  - *Ex Vivo* Diagnostic Screening
  - *In Vivo* Diagnostic Imaging
  - *In Vivo* Guided Therapy

Innovation Results:
MGH/VisEn/SIEMENS – *In-Vivo* Imaging



7] COLOR-ENCODED near-infrared fluorescence image of a mouse, implanted with two different human breast tumors, differing in tissue invasiveness. The mouse was injected with a fluorochromes-labeled smart probe, activated by cathepsin-B. The agent is more activated in the more invasive right tumor. (Image courtesy of Ralph Weissleder, CMIR).

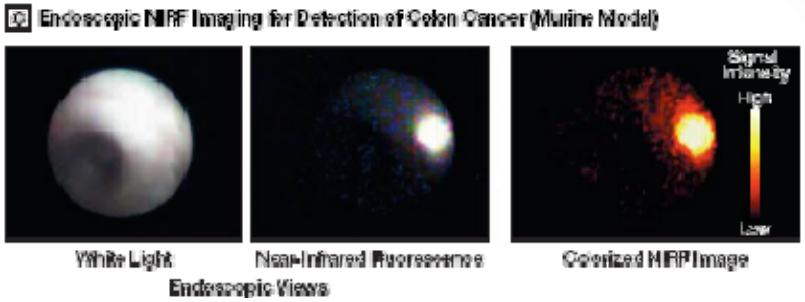


Table 2. Optical/NIRF and Ultrasound Molecular Imaging Agents*

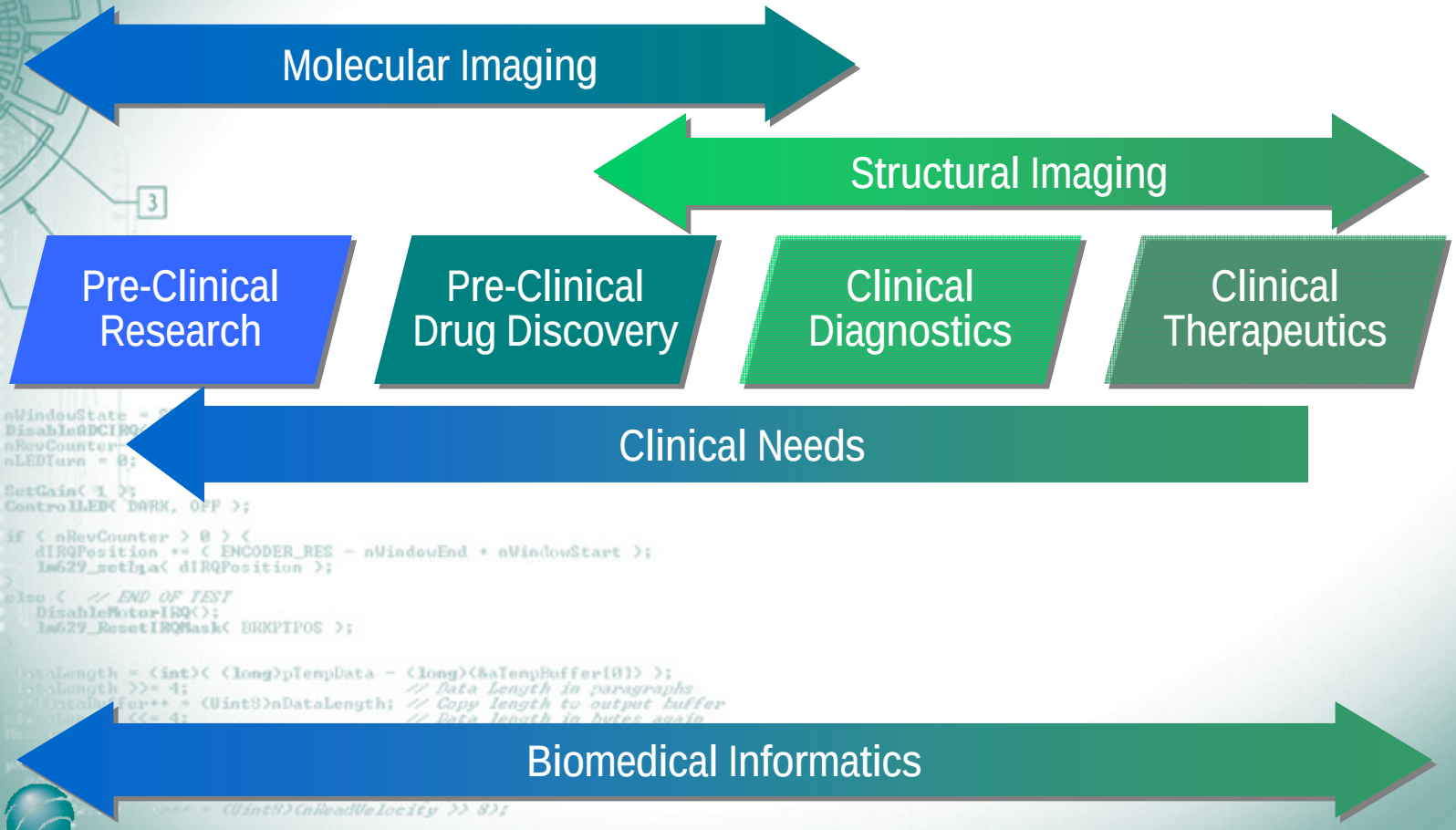
Disease	Imaging Technology	Imaging Agent	Clinical Application
Cancer	Optical/NIRF	Cathepsin B	Many cancers
		Matrix metalloproteinases	Many cancers
		Targeted fluorochromes (her2neu, annexin A5, etc)	Many cancers
	Ultrasound	Integrin $\alpha_v\beta_3$	Angiogenesis
Atherosclerosis (vulnerable plaque)	Optical/NIRF	Cathepsin B	Inflammation
		Matrix metalloproteinases	Inflammation
		Annexin A5	Apoptosis
		Fibronectin	Angiogenesis
		Vascular cell adhesion molecule 1	Inflammation
	Ultrasound	Intercellular adhesion molecule	Inflammation
		Vascular cell adhesion molecule 1	Inflammation
Thrombosis	Optical/NIRF	Plasmin	Acute thrombi
		Factor XIIIa	Acute thrombi
	Ultrasound	Fibrin and fibrinogen	Acute/subacute thrombi
		Tissue factor	Acute thrombi
		Activated integrin $\alpha_{IIb}\beta_3$	Platelets
Neurological	Optical/NIRF	Pittsburgh compound B	Alzheimer dementia
Arthritis	Optical/NIRF	Cathepsin B	Inflammation
		Diphosphonate	Osteoblast activity

Abbreviation: NIRF, near-infrared fluorescence.
*Animal experiments only to date, with clinical trials anticipated. Imaging agents were compiled from a literature search in PubMed. The list is meant to be representative and not exhaustive. For more in-depth information on recent advances, please consult references 4, 7, 17, and 35. Imaging agents that do not exhibit cellular uptake/binding are excluded.

Innovation Commercialization

- VisEn has received major equity investments from Siemens
- Major pharmaceutical partners for Drug Discovery
  - Novartis
  - Others (undisclosed)
- Commercially available bonSAI Imaging System through Siemens for Pre-Clinical Research and Drug Discovery
- "The adaptation of fluorescent optical techniques to diagnostic imaging is now changing the way we visualize molecular processes in vivo, and ultimately, in the clinic." *Dr. Ralph Weissleder, MD, PhD, Director CMIR*

Convergence Around a Clinical Need Example



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Innovation Source:

Center for Integration of Medicine and Innovative Technology
MGH, BWH, Harvard Medical, MIT, Draper Labs

- Multi-disciplinary organization tapping talent at Major Research Hospitals, Medical andTechnology Research Centers
- Example Program: Vulnerable Plaque “Living Laboratory”
- Unique multi-organization cooperative environment, guided by clinical needs and *clinical realities*

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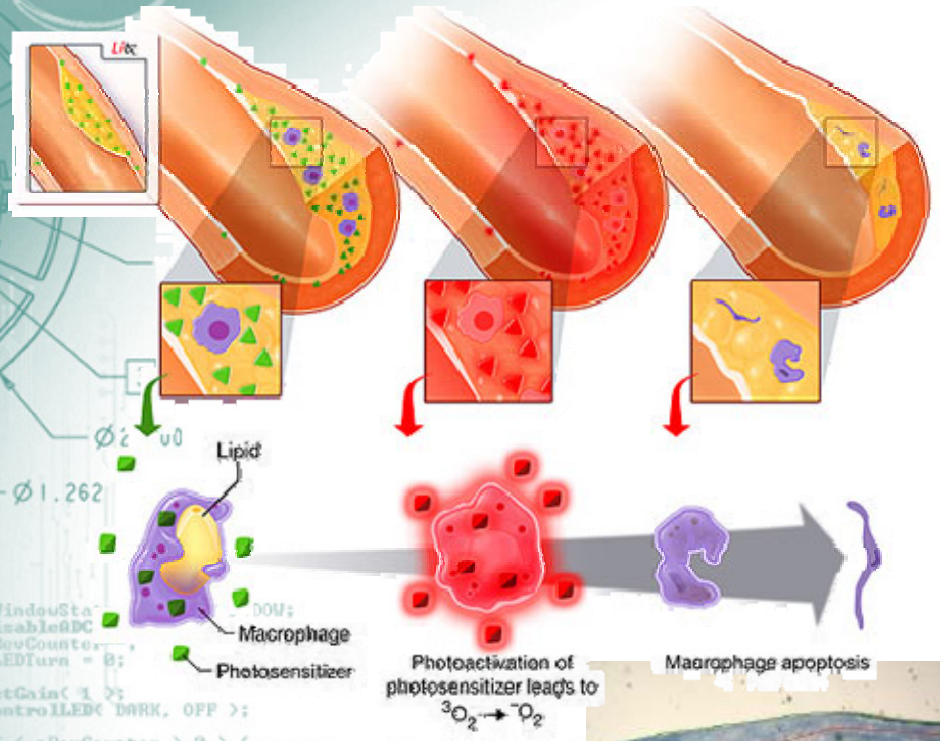
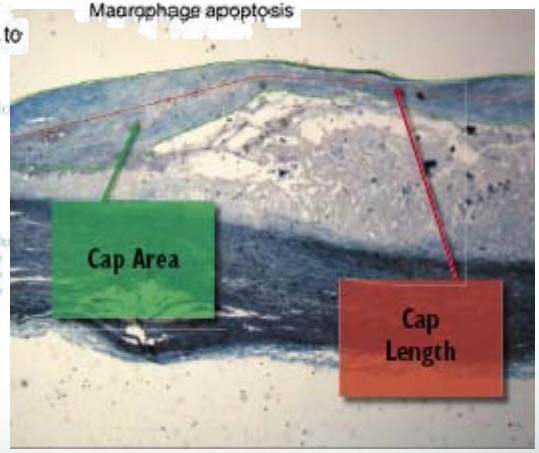
Innovation Results: Emerging *In Vitro* Diagnostics, *In Vivo* Imaging and Therapy

- More than 20 Collaborative Programs Underway
- Major Pharma, MedTech and Startup Participation
  - J&J Cordis
  - Medtronic
  - Guidant
  - Boston Scientific
  - GE Amersham
  - Terumo
  - InfraReDx
  - Epix Pharmaceuticals
  - Pharmacyclics
  - Miravant
  - Thermacore/BMS
  - Light Sciences
- Convergence of Screening, Imaging and Therapeutic Options
  - In-vitro Screening
  - Non- and Minimally-Invasive Intra-vascular Imaging
  - Therapeutic Agents (some with Intra-vascular Activation)

Innovation Results:
Pre-Clinical and Clinical Trials





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Innovation Commercialization

- Initial Pre-Clinical Commercialization of Diagnostics and Therapies

  => Heavily Guided by Clinical Community

- Strong Cooperation Among Major Pharma and MedTech Players
- Major Clinical Trials coordinating Diagnostics and Therapeutics
- Broad Intellectual Property Cross-Licensing
  - Low Risk Screening drives need for Interventional Diagnosis
  - Interventional Diagnosis drive Therapies
  - Many Therapies rely on intra-vascular technologies
  - Availability of Therapies drive use of Screening

Questions and Discussion

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