

National Cancer Institute

# NCI Director's Update

**Dr. John E. Niederhuber**  
Director, National Cancer Institute

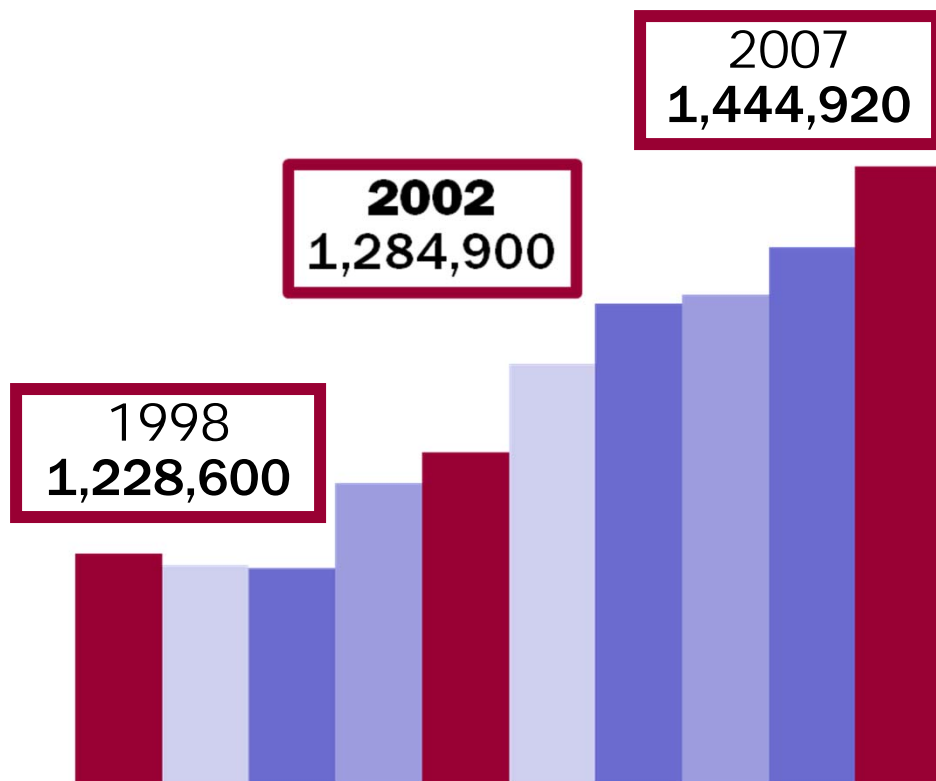
Board of Scientific Advisors  
March 3, 2008

U.S. DEPARTMENT  
OF HEALTH AND  
HUMAN SERVICES

National Institutes  
of Health

# Why What We Are Doing is So Important

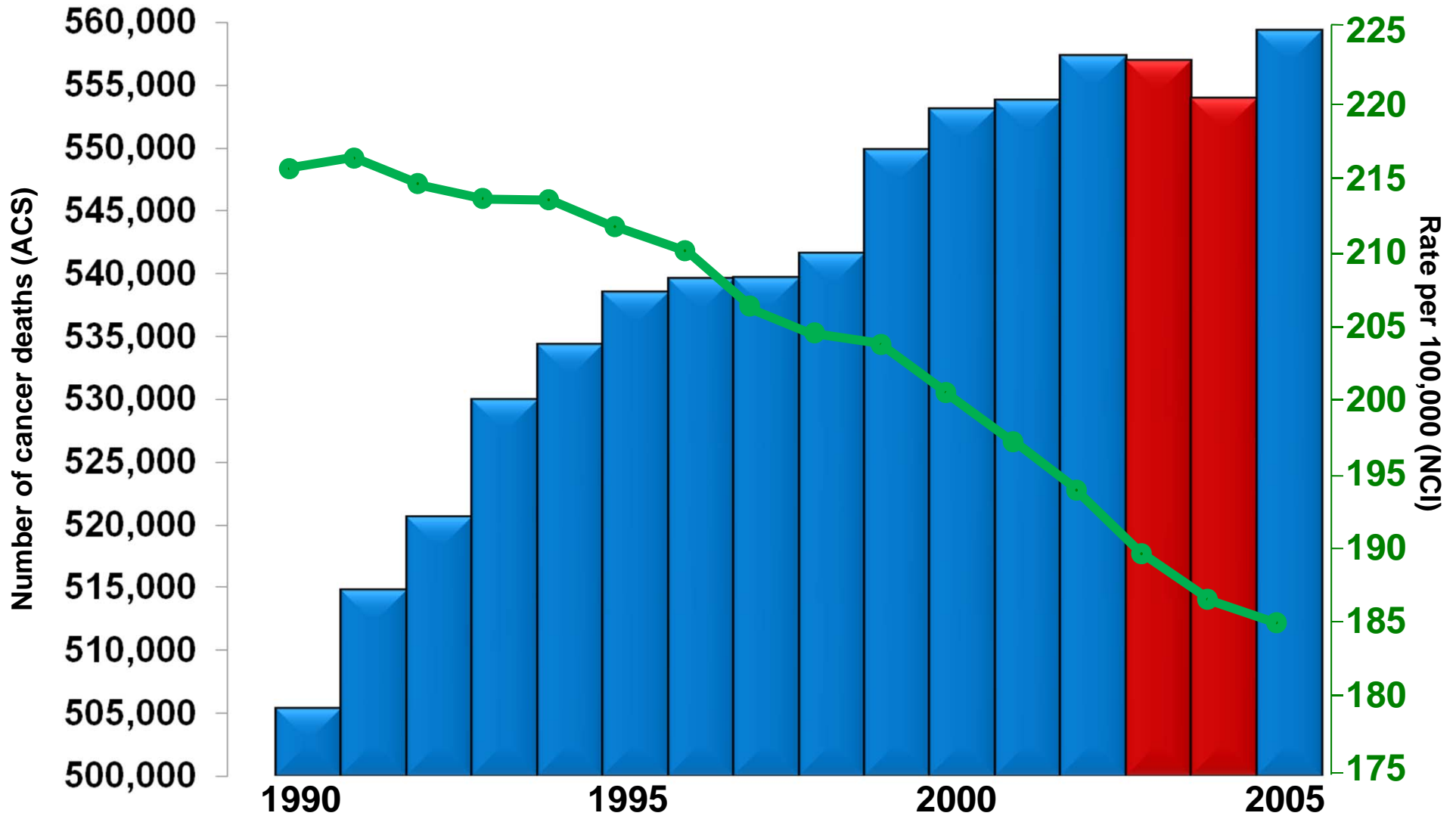
## Human and Economic Burden of Cancer



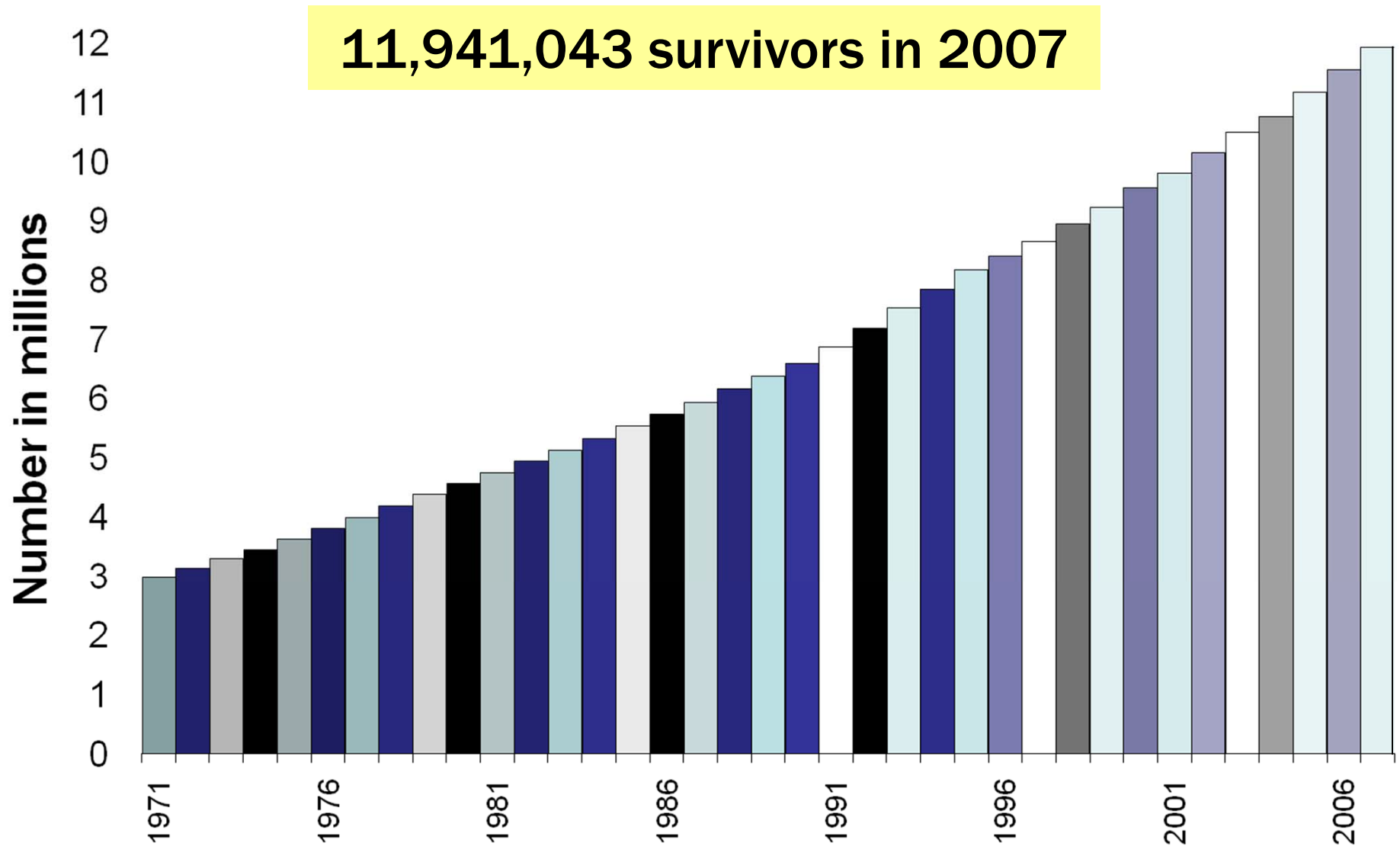
Estimated # of New U.S. Cancer Cases

- 1,444,920 Americans were diagnosed in 2007
- 559,650 died of cancer in 2007
- \$206.3 billion spent on healthcare costs for cancer in 2006
- 47 million Americans lack health insurance

# Cancer Death Rates

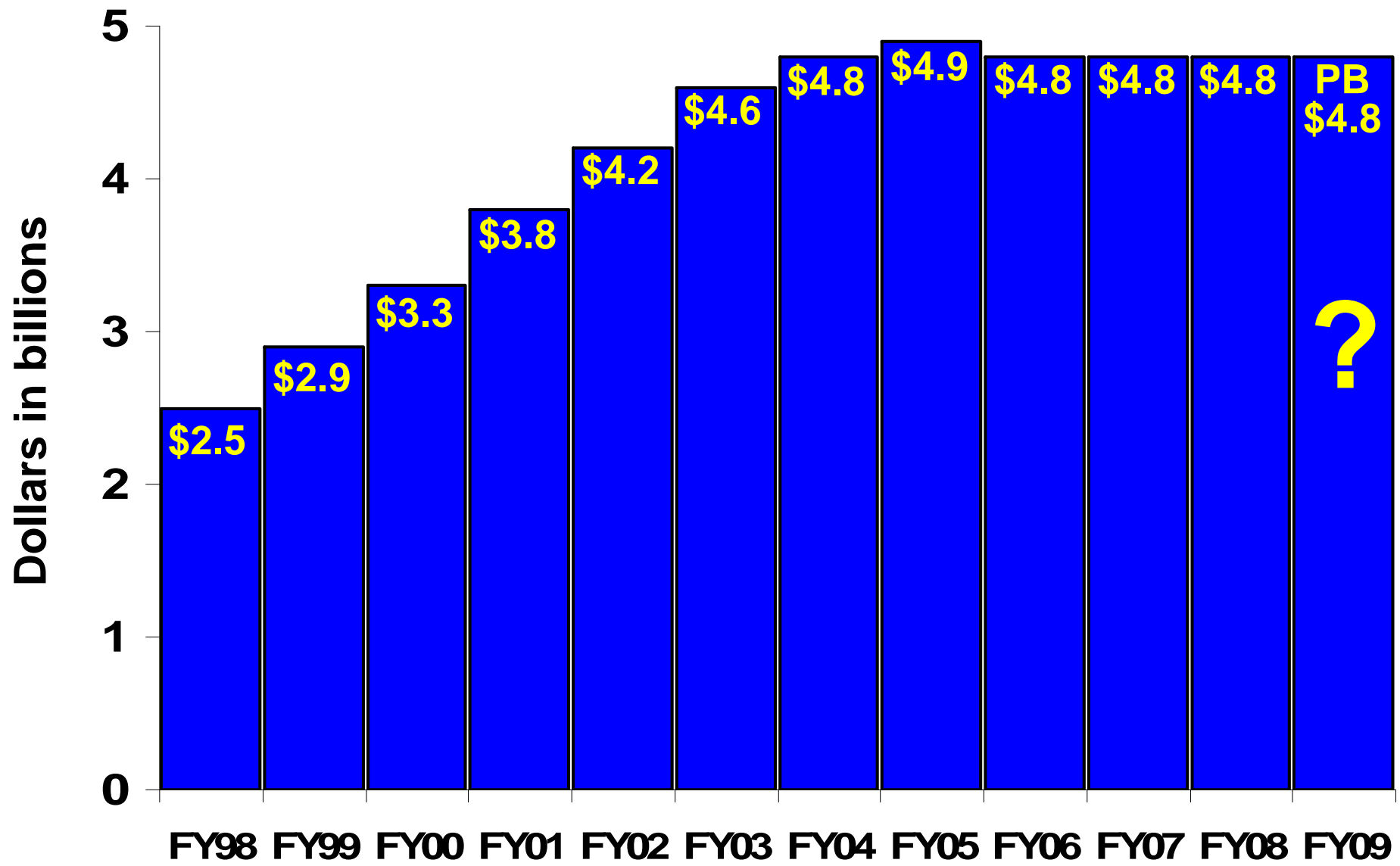


# Estimated Number of Cancer Survivors in the United States

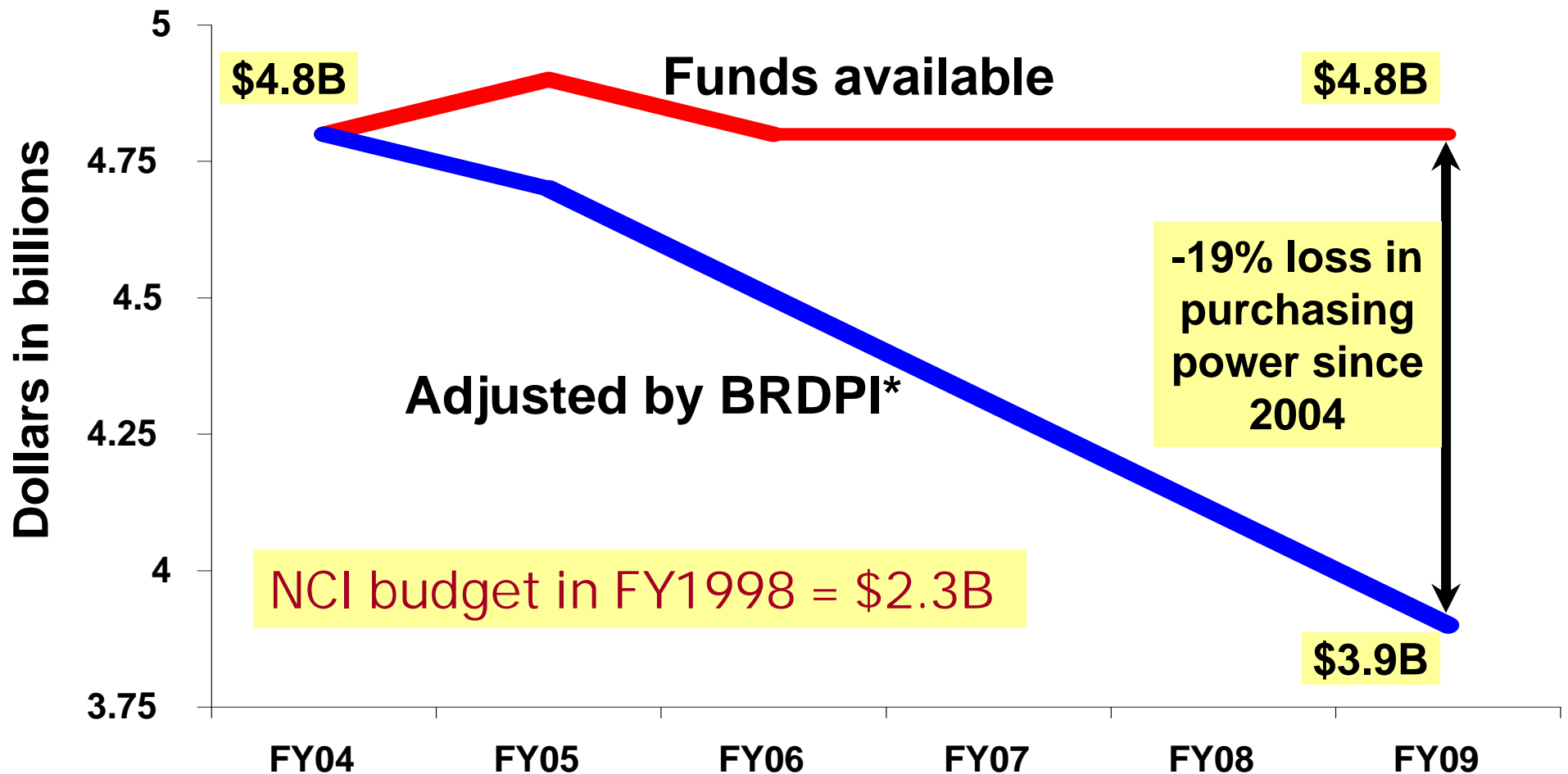


# NCI's Congressional Appropriations

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# NCI's Challenge



\* BRDPI: Biomedical Research and Development Price Index  
(<http://officeofbudget.od.nih.gov>)

# Director's Update

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- **NCI FY08 budget**
- **President's budget FY09**
- **Some thoughts about the future**

# NCI FY 2008 Operating Budget Development

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<b>FY 2007 operating budget</b>	<b>\$4,797,639</b>
<b>FY 2008 appropriation</b>	<b>\$4,805,088</b>
<b>Difference '07 to '08</b>	<b>\$7,449</b>
<b>Percent Change '07 to '08</b>	<b>+0.16%</b>

**(dollars in thousands)**



# NCI FY 2008 Operating Budget Development

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	<u>Amount (in thousands)</u>	<u>Percent change</u>
<b>Subtotal Available</b>	\$7,449	0.16%
<b>Less Est. NIH Taps/Assessments</b>	<b>-20,000</b>	
• Potential NIH Director's 1% Transfer	?	
• Potential DHHS Secretary's Transfer	?	
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<b>Subtotal Available</b>	<b>-12,551</b>	<b>-0.26%</b>

# NCI FY 2008 Operating Budget Development

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	<u>Amount</u> <u>(in thousands)</u>	<u>Percent</u> <u>change</u>
<b>Subtotal Available</b>	- \$12,551	-0.26%
<b>NCI-wide Requirements:</b>		
• Mandated Salary Increases	- 21,500	
• Rent/Lease/Utilities/Renovations Incr	- 10,000	
• Small Business Program Increase	0	
<b>NCI Director's Reserve</b>	<u>- 25,000</u>	
<b>Subtotal Available</b>	- 69,051	-1.44%

# NCI FY 2008 Operating Budget Development

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	<u>Amount (in thousands)</u>	<u>Percent change</u>
<b>Subtotal Available</b>	- \$69,051	- 1.44%
<b>Partial Restoration of Cuts</b>		
• Centers	- 7,855	
• SPORES	-3,588	
• Coop Groups/CCOPs	-8,504	
• Infrastructure Restorations/Increases	-6,000	
<b>Subtotal Available</b>	<b>-94,998</b>	<b>- 1.98%</b>

# NCI FY 2008 Operating Budget Development Process

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- NCI leaders evaluated programs with an eye toward reduced or flat budgets ahead
  - FY08 operating budget target for each Division, Office and Center (DOC) is based on a 3% reduction
- Created a pool of funds for NCI-wide mandatory increases and reallocation for specific initiatives

# NCI FY 2008 Operating Budget Development

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	<u>Amount (in thousands)</u>	<u>Percent change</u>
<b>Subtotal Available</b>	- \$94,998	- 1.98%
<b>Potential Recoveries/Redeployments:</b>		
• Phaseouts/Reductions Res DOCs	49,382	
• Phaseouts/Reductions Infrastructure	6,778	
• Noncompeting RPGs	46,228	
• Competing RPGs	8,136	
• NCI-Frederick Redeployment	40,000	
	<hr/> <hr/>	
<b>Available for New Initiatives/ Expansions/Restorations</b>	<b>\$55,526</b>	

# NCI FY 2008 Operating Budget: NCI Operating Policies

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## NCI operating policies

- **1% inflationary adjustments on non-competing grants**
  - **~2% decrease from commitment for non-modular grants**
- **No cut to modular non-competing grants**
- **NCI to award fewer competing RPGs than FY 2007 (1,312 to 1,283)**

# NCI FY 2008 Operating Budget: NCI RPG Policies

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## NCI RPG policies

- **Type-2** (competing continuing grants) will receive **3%** above current levels
- **Type-2 modular grants** recommended for **7 modules or fewer** will receive **5%** above current levels
- **Type-1** (new competing grants) will be cut **~17%**

# NCI FY 2008 Operating Budget: NCI RPG Paylines

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## NCI RPG Paylines

- R01: 12<sup>th</sup> percentile (14)
- \*R01s: 19<sup>th</sup> percentile (will hit NIH target)
- Large R01s (over \$700K):
  - 14<sup>th</sup> percentile for 1<sup>st</sup> and 2<sup>nd</sup> rounds
  - TBD for 3<sup>rd</sup> round
- P01: Selected on a case-by-case basis



# Examples of Downsized and Stopped Programs

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## Office of Centers, Training, and Resources

- **Integrating Aging and Cancer Research (co-funded with NIA)**
  - NCI funding of \$4M-\$5M will not be renewed
- **Supplements for Imaging Response Assessment Teams in Cancer Centers**
  - NCI funding of \$2M will not be renewed

# Examples of Downsized and Stopped Programs

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## Div. of Cancer Control & Population Sciences

- **Transdisciplinary Tobacco Use Research Centers**
  - FY2008 is final year of RFA, funded at \$7.2M. No proposed RFA renewal
  - NCI is joining a NIDA PA; For TTURC program, anticipate spending \$2M-4M, rather than \$7.2M/yr
- **Long Term Cancer Survivors research RFA**
  - FY2008 funding reduced by \$1.7M

# Examples of Downsized and Stopped Programs

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## Division of Cancer Prevention

- **CCOP cancer treatment trial accrual**
  - FY05: 7,948 patients
  - FY06: 6,402 patients
  - FY07: 6,100 patients (estimate)
- **CCOP cancer prevention & control trials:**
  - FY05: 5,211 patients
  - FY06: 4,994 patients
  - FY07: 4,500 patients (estimate)

# Examples of Downsized and Stopped Programs

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## Division of Cancer Treatment and Diagnosis

- **CTEP Interdisciplinary Research Teams for Molecular Target Assessment**
  - Eliminated in FY07; \$1.4M
- **Cancer Imaging Program's Development of Contract Imaging Drugs and Enhancers**
  - Eliminated in FY07; \$1.6M
- **Cancer Diagnosis Program: breast and prostate cancer tissue resources unfunded or eliminated**
  - Prostate eliminated FY07; breast unfunded extension (combined max. funding \$3.25M/yr)

# Examples of Downsized and Stopped Programs

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## Division of Cancer Treatment and Diagnosis

- **Data Resource for Analyzing Blood and Marrow Transplants**
  - **Approved for funding at proposed level for FY08 (\$600K)**
  - **~80% of proposed level for FY09 – FY12 (savings of approximately \$470K each fiscal year)**

# FY 2009 President's Budget

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<b>FY08 NCI appropriation</b>	<b>\$4,805,088</b>
<b>FY 2009 PB for NCI</b>	<b>\$4,809,088</b>
<b>Difference '08 to '09</b>	<b>\$4,000</b>
<b>Percent Change '08 to '09</b>	<b>+0.1%</b>

**(dollars in thousands)**

# TRWG Implementation

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- Dr. Lynn Matrisian (co-chair of the TRWG) now at NCI on an IPA
- Integrating with the CCCT
- **Translational Research Operation Committee planned**
  - Established under the Clinical Trials Advisory Committee (a Federal Advisory Board)

# Translational Research Working Group Goals

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- Improve coordination and collaboration and instill a culture of active, goal-oriented management
- Improve identification of the most promising early translation research opportunities
- Tailor new and existing programs to facilitate early translational research progress
- Enhance operational efficiency and effectiveness



# Office of Centers, Training, and Resources

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- **Cancer Centers Program**
  - Remain in the Office of the Director
- **Organ Systems Branch (SPOREs)**
  - Moving to the Division of Cancer Treatment and Diagnosis
- **Training Branch**
  - Transition specific programs to the Divisions

# SPOREs Leadership

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- **Drs. Jim Doroshow and John Niederhuber will oversee the SPOREs**
  - Continue monthly teleconference calls with SPORE Executive Committee
- **Dr. Toby Tucker Hecht named acting head during national/international search for new SPORE director**
- **Dr. Jorge Gomez will lead a new NCI initiative to enhance global research and clinical trials participation in Central and South America**

# Role of Clinical Research Center

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## NCI Initiatives

- Continue to strengthen Medical Oncology
- Recruiting new chief of Laboratory of Pathology
- Pathology space renovations in Bldg 10
- Developing an Oncology Imaging Center
- Exploration of a Satellite Center at Suburban Hospital
- Strengthening fellowship training
- Participation in rare diseases clinic

# Annual Translational Research Meeting

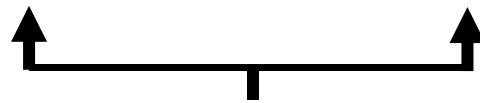
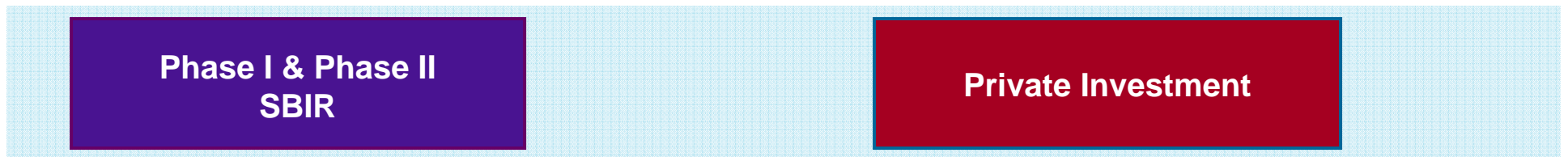
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- **Replace the summer SPORE meeting with an annual meeting**
- **Co-Chaired by Drs. Sheila Prindiville and Lynn Matrisian**
- **Planned for the Fall 2008 in Washington, D.C.**

# The SBIR Bridge Award in Drug Development

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The “**Valley of Death**”  
is the problem

# Theoretical Physics

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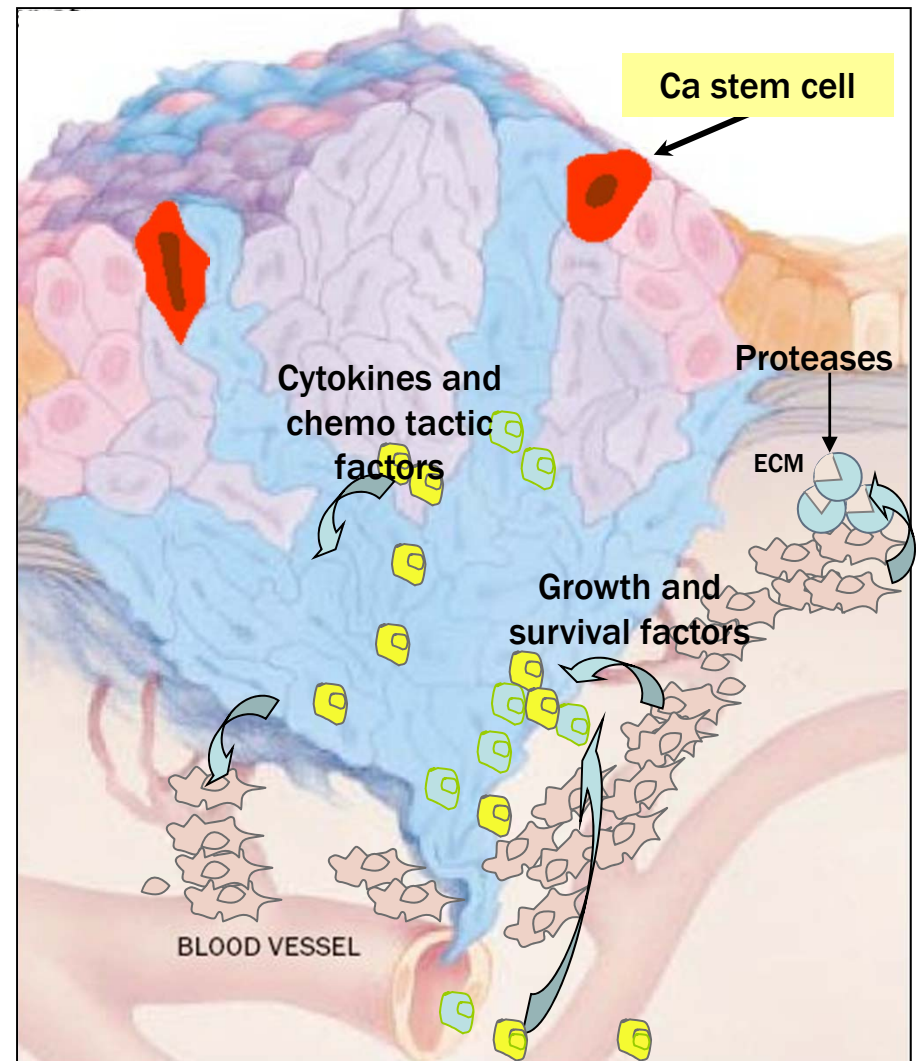
- Feb. 26-28, 2008
- Workshop to explore opportunities to incentivize collaborations
- Leaders in physics, chemistry, mathematics and cancer research



# Tumors are “organs” composed of many interdependent cell types

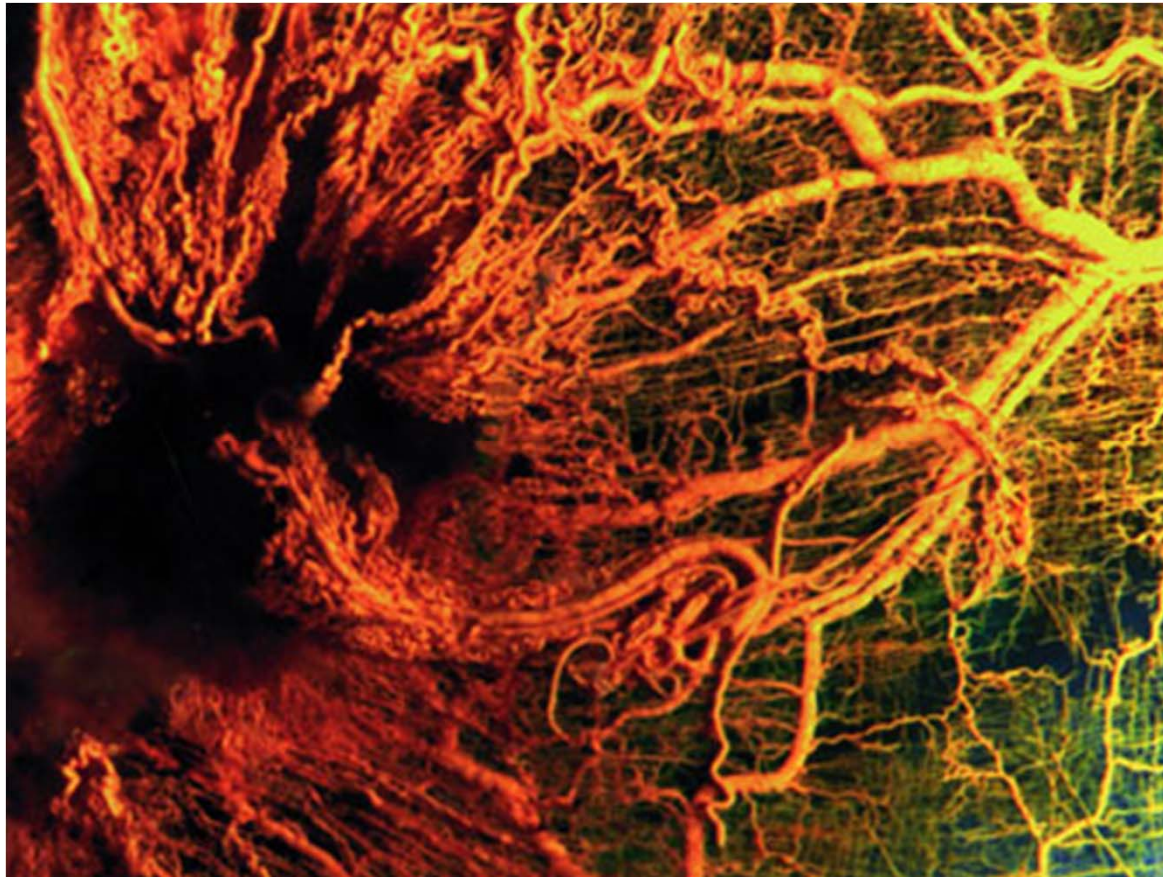
Factors produced in cells within the tumor microenvironment can alter aspects of tumor cell behavior

- Growth factors produced in adjacent cells promote cell proliferation and survival
- Cytokines and chemo tactic factors produced by inflammatory cells and other stroma promote cell migration and invasion
- Proteases produced by the mE break down basement membrane, altering the architecture of tissue structures and migration/invasion of tumor cells

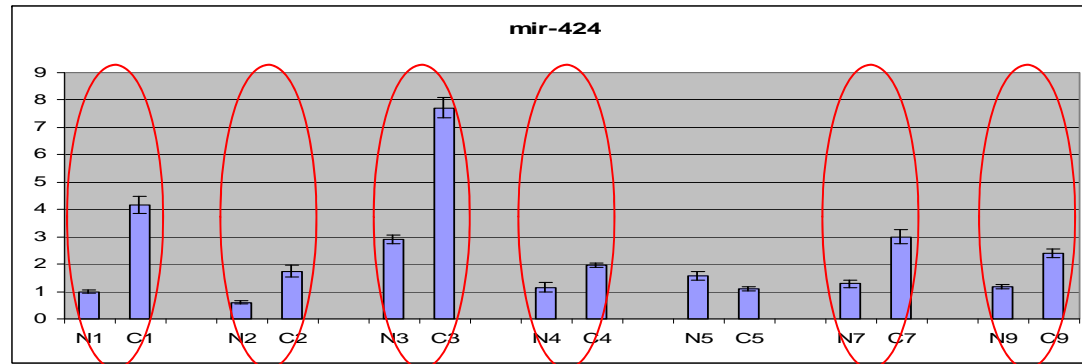




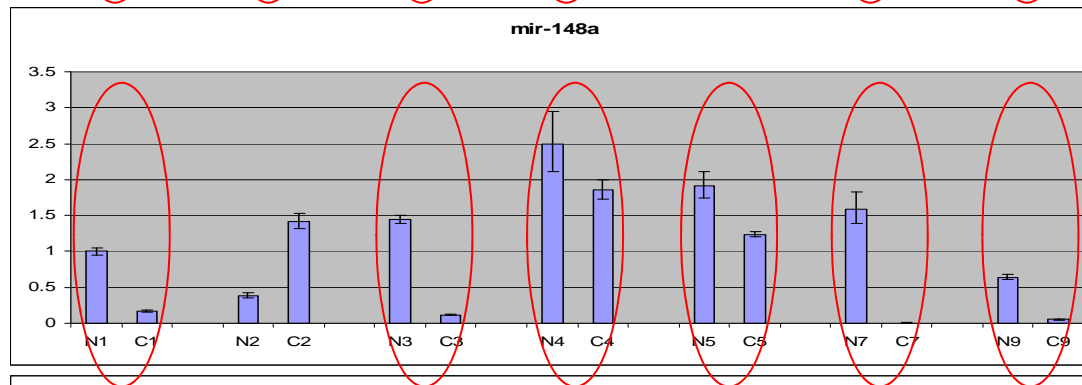
# New Blood Vessel Growth Into Tumor



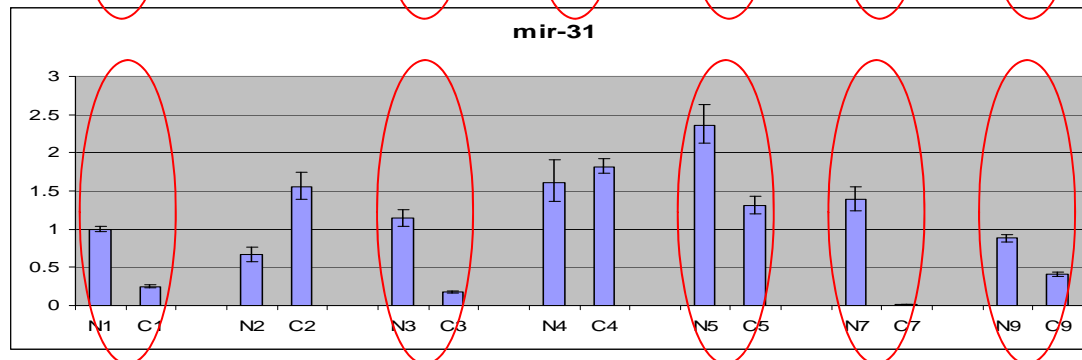
# Real-time PCR validation of microRNA profiling data



**Upregulated in cancer fibroblasts**



**Downregulated in cancer fibroblasts**



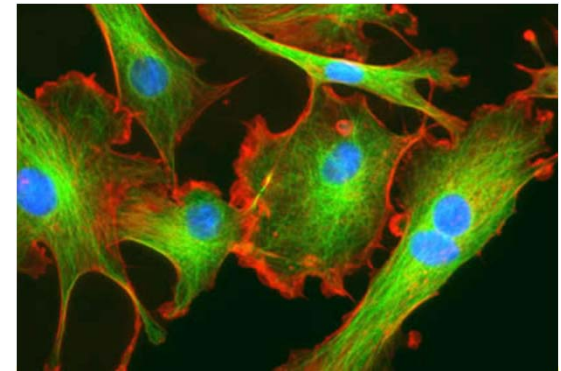
**Downregulated in cancer fibroblasts**

# MicroRNA profiling results

Name	P-Value	Average Consistent Fold Change
hsa-miR-503	0.0072	-1.88
hsa-miR-424	0.0015	-1.81
hsa-miR-146a	0.0015	-1.80
hsa-miR-181b	0.0072	-1.80
hsa-miR-542-3p	0.0072	-1.57
hsa-miR-638	0.0072	-1.54
hsa-miR-29b	0.0266	-1.50
hsa-miR-127	0.0266	1.53
hsa-miR-148a	0.0266	1.57
hsa-miR-224	0.0002	1.61
hsa-miR-31	0.0072	3.66

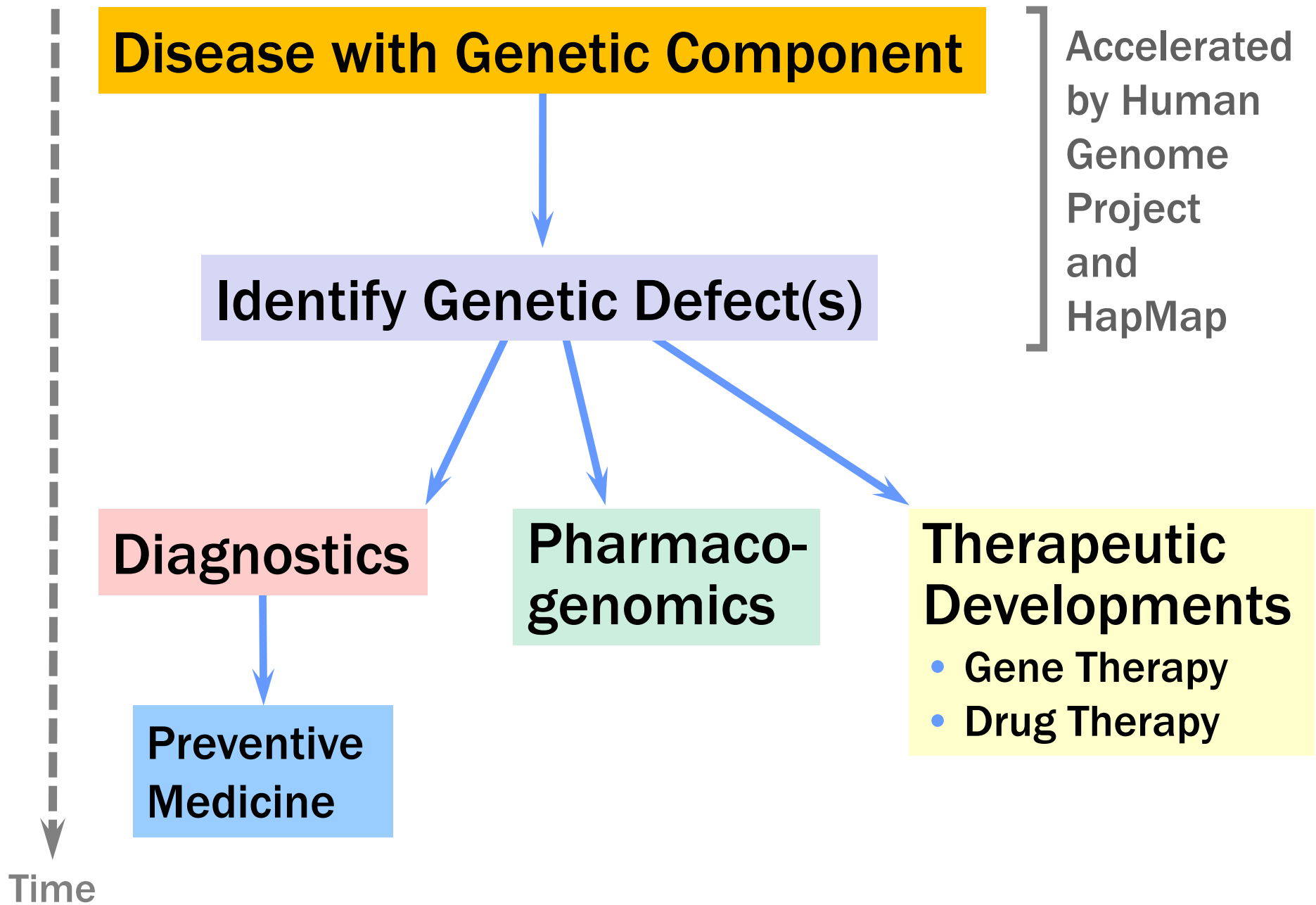
Higher in cancer fibroblasts

Higher in normal fibroblasts

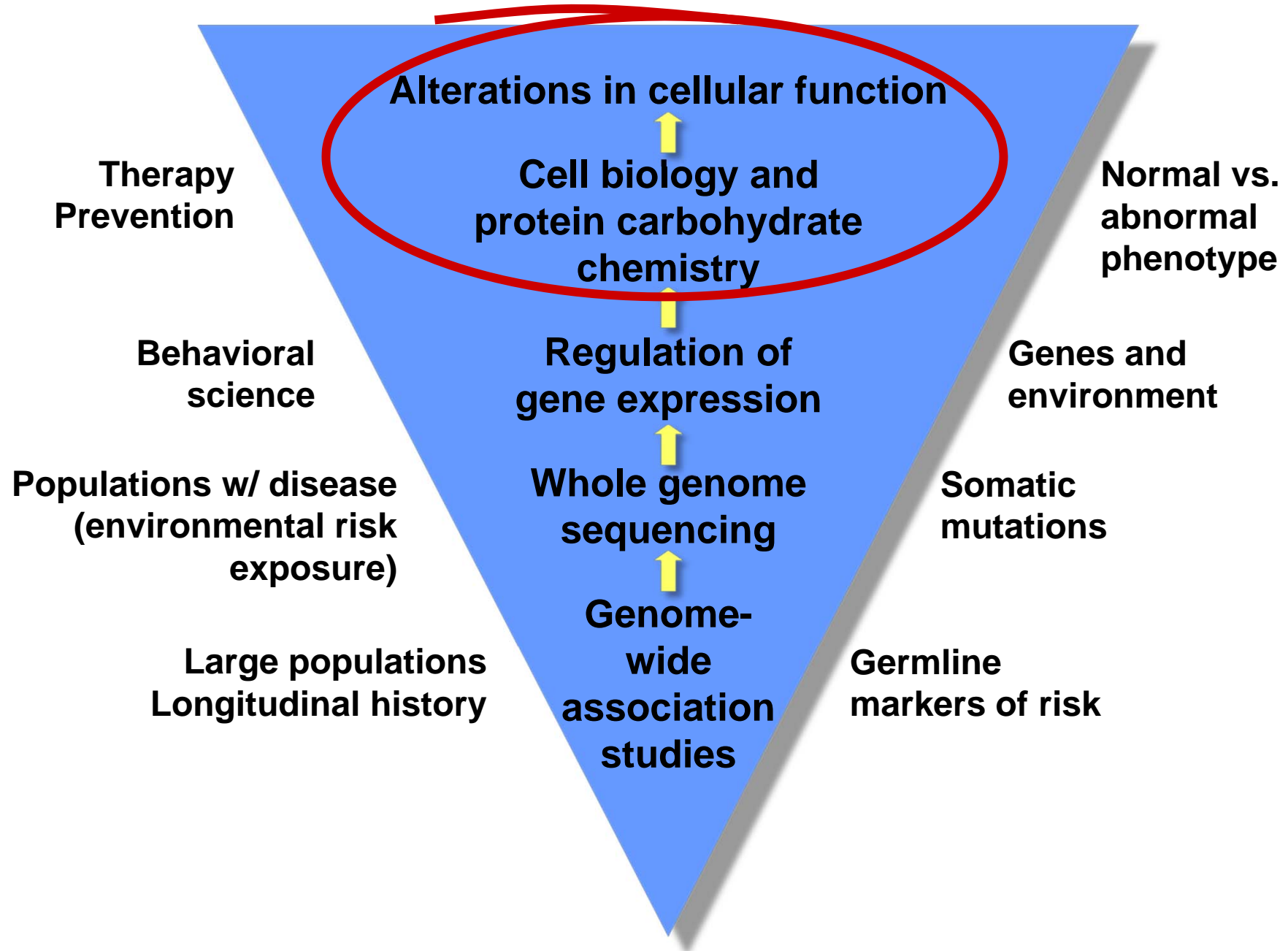


Out of 553 human microRNA spotted on the chip, 11 showed more than a 1.5-fold difference between normal and cancer fibroblasts with the P-value < 0.027

Niederhuber Lab



# Functional Genomics



# A Physicist's Insight into Biology

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“It is not that the subject  
(biology) was simple enough  
to be explained by  
mathematics, but rather that  
it was much too involved to  
be fully accessible to  
mathematics.”

$$\hat{H}|\psi\rangle = i\hbar\frac{d}{dt}|\psi\rangle$$



Erwin Schrödinger

1944

**“Biology is more like history than it is like physics. You have to know the past to understand the present, there is no predictive theory of biology just as there is no predictive theory of history. The reason is the same; both subjects are too complicated for us.”**

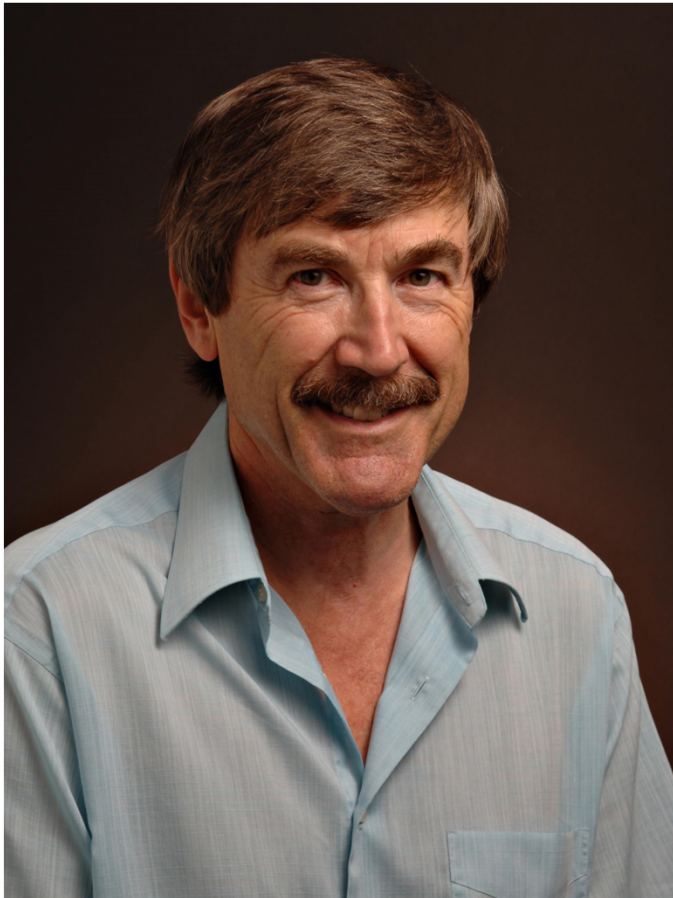
**Carl Sagan**

What can physics,  
physical chemistry,  
and applied  
mathematics bring  
to cancer biology?



# Paul Davies, Ph.D.

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- **Director**  
**Beyond Institute**  
**Arizona State University**
- **Keynote Presentation:**  
**“Confronting Complexity:  
Cancer at the  
Intersection of Physics  
and Biology”**

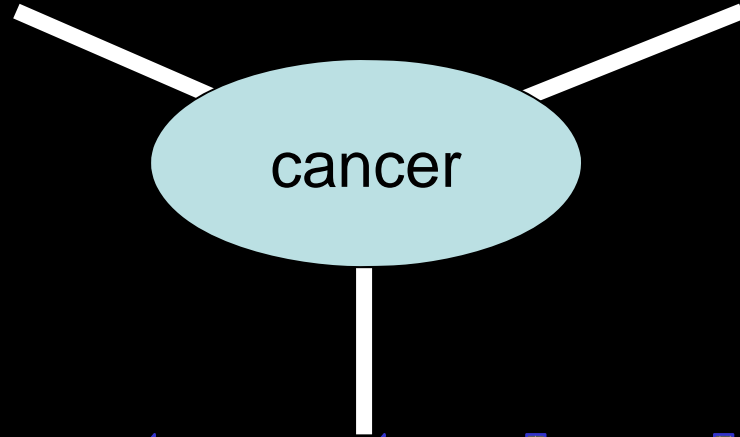
# The technology of the complex future

*biotechnology*

*nanotechnology*

cancer

*quantum technology*



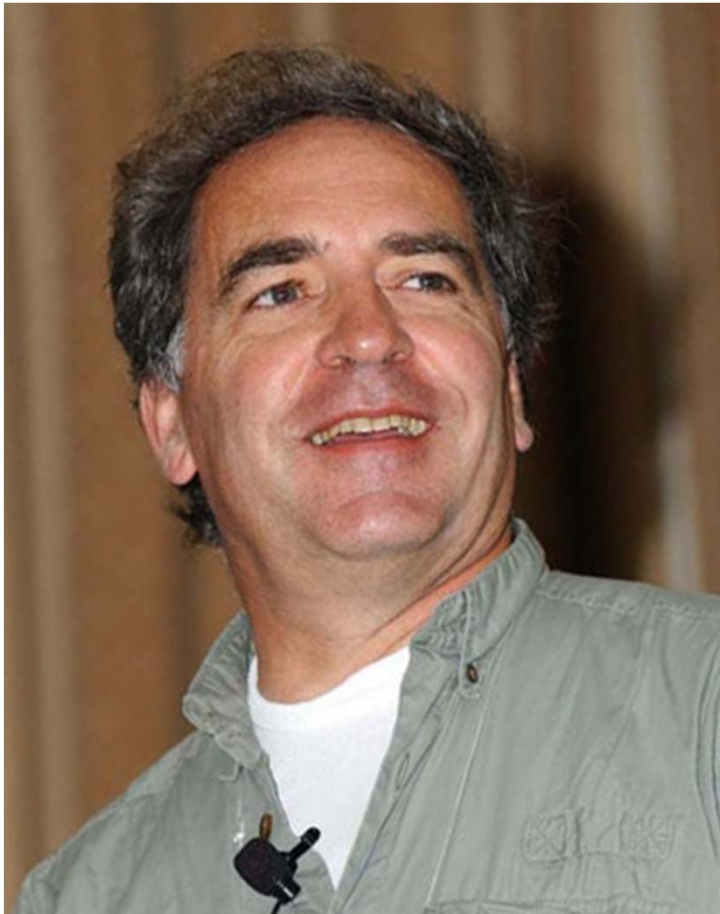
# Theoretical physics

- New conceptual insights into complex systems
- Experience with modeling computational complexity
- Ability to extract a signal from confusing noise
- Ability to “stand back” and see the system as a whole
- Tendency to ask really dumb questions, seemingly without embarrassment
- Salamander limb regeneration
- How do cells stick together, and why do metastasized cells come unstuck?
- Tolerance of “wild ideas”



# Robert Austin, Ph.D.

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- **Professor of Physics**  
Princeton University
- **Keynote Presentation:**  
“21st Century Physics—  
Relevant Intersections  
With Barriers in  
Oncology”

# Donald Coffey, Ph.D.

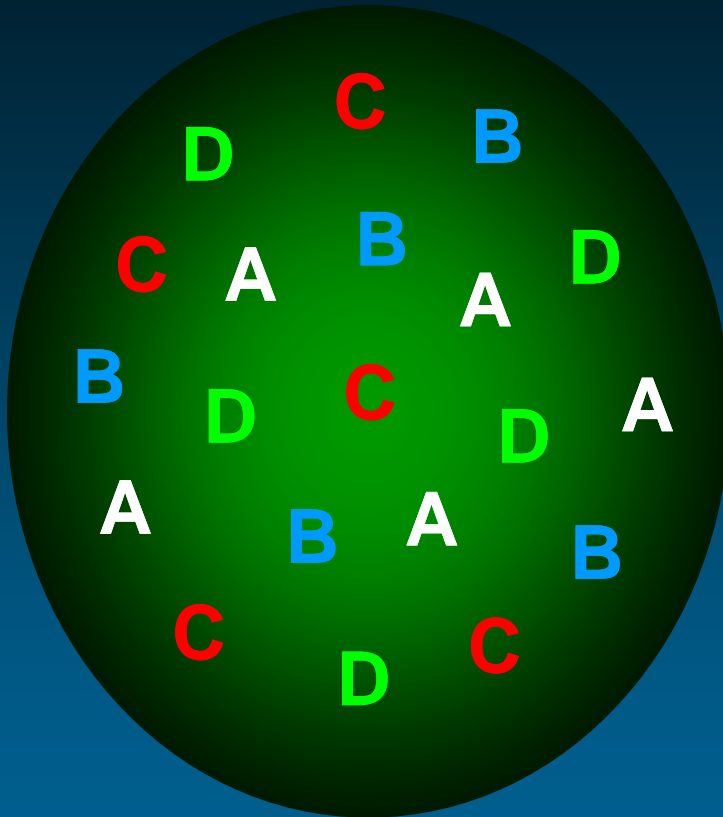
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- Professor of Urology; Oncology; Pathology and Pharmacology; and Molecular Sciences  
*Johns Hopkins Univ.*
- Keynote Presentation: “The Physical Sciences and Cancer Biology—Early Glimpses Across the Frontier”

# TWO TYPES OF INFORMATION FLOW WITHIN A CELL

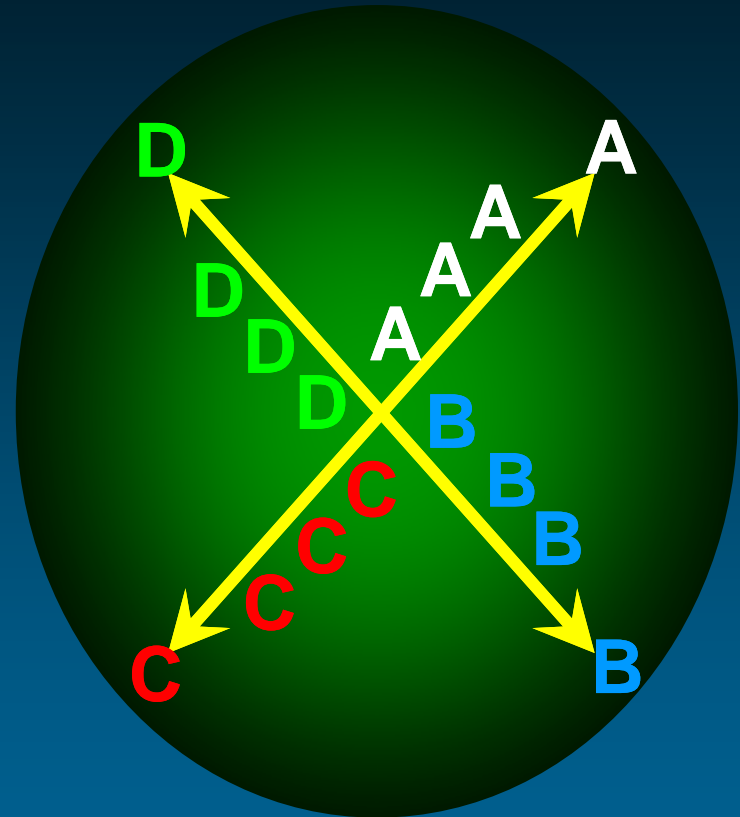
## DIFFUSION



Soluble

GRADIENTS  
OSCILLATORY  
B-Z Reactions

## VECTORIAL



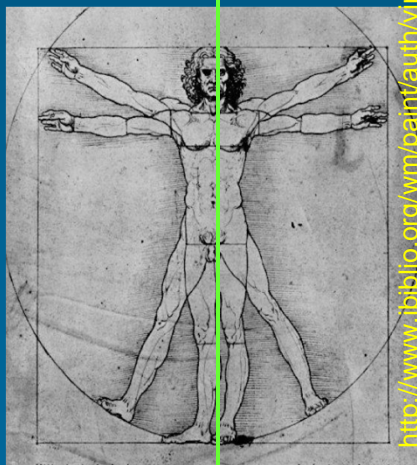
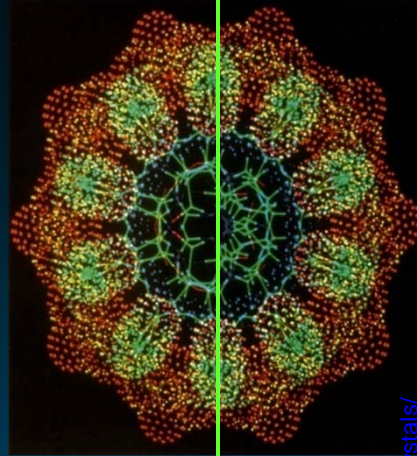
Structural

CHEMOMECHANICAL  
VIBRATIONAL  
TENSEGRITY

End view  
of DNA  
helix

(10bp)  
Snowflake

Human



?

Thermodynamics  
Complexity  
Simplicity  
Symmetry  
Self Organization  
Information  
transfer  
Far from  
equilibrium  
Emergent property  
Non-linear  
Fractal  
Chaos  
Order  
Increased rate of  
entropy  
Evolution

CANCER

# Ideas for Involving the Physical Sciences in Cancer Research

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- We lack a field of **Theoretical Cancer Biology**
- Tumor cell complexity in association with the **microenvironment requires mathematical models** (cell communication, metastasis)
- **Impact of basic physical principles and laws** on cancer (mechanical forces, energy and energy transfer, cell shape, dimensions of time)
- The role of **tumor cell evolution**





