

TRANSLATIONAL RESEARCH: MAKING CANCER HISTORY

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April 28, 2005

CANCER OCCURS FREQUENTLY

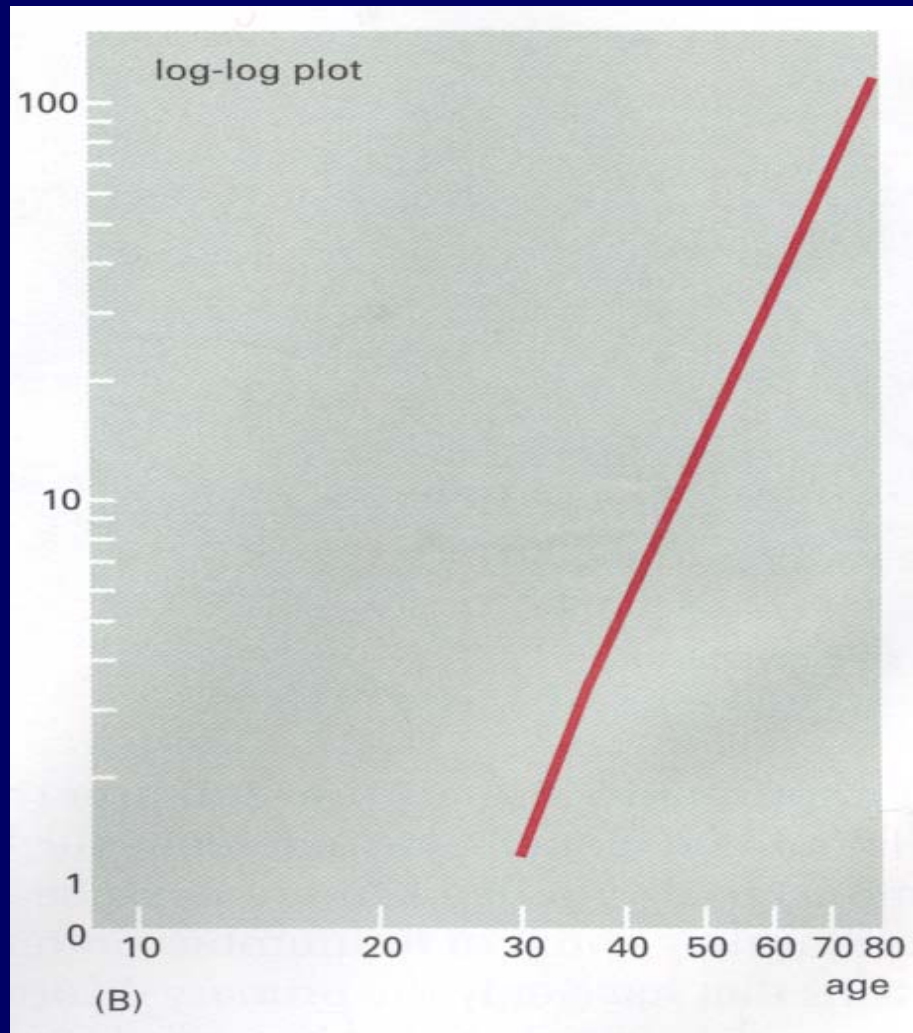
- **1 in 3 Lifetime Risk**
- **1.2 million New Cases in the United States Annually**
- **563,000 Deaths Annually**

ARE WE WINNING THE WAR ON CANCER?

- **Since 1997, more than half of patients with potentially lethal cancers have been cured.**
 - **Early detection**
 - **More effective surgery, radiotherapy and chemotherapy**
- **Aging of our population may erode these gains**

CANCER IS A DISEASE OF AGING

- Cancer can occur at Any Age, but is Most Frequent in Older People
- Accumulated Mutations
 - Wear and Tear
 - Environmental Insults
- Evolution protects Us Until Age 30



OUR WORLD'S POPULATION IS GROWING AND AGING

Between 1998 and 2025:

- **Population**
 - 5.8 Billion to 8.0 Billion (37%↑)
- **People >65 Years**
 - 390 Million to 800 Million (105%↑)
- **Life Expectancy**
 - 65 Years to 73 Years (12%↑)
- **Age at Death >65**
 - 43% to 63% (46% ↑)

GROUNDS FOR OPTIMISM

- **Omic Revolution**
- **Computer Revolution**
- **Informatic Revolution**

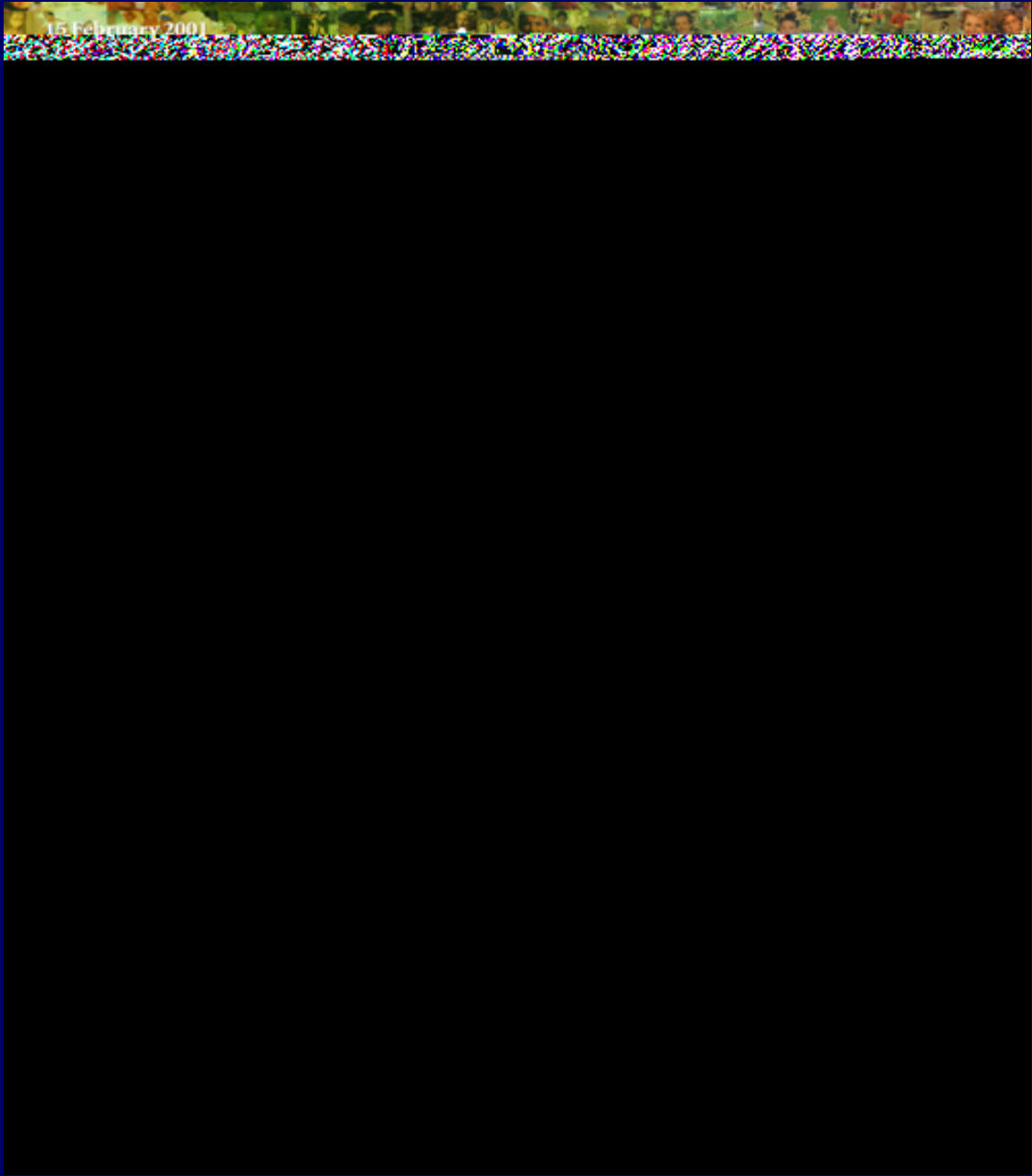
Science

10 February 2001

Vol. 291 No. 5507
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THE HUMAN GENOME

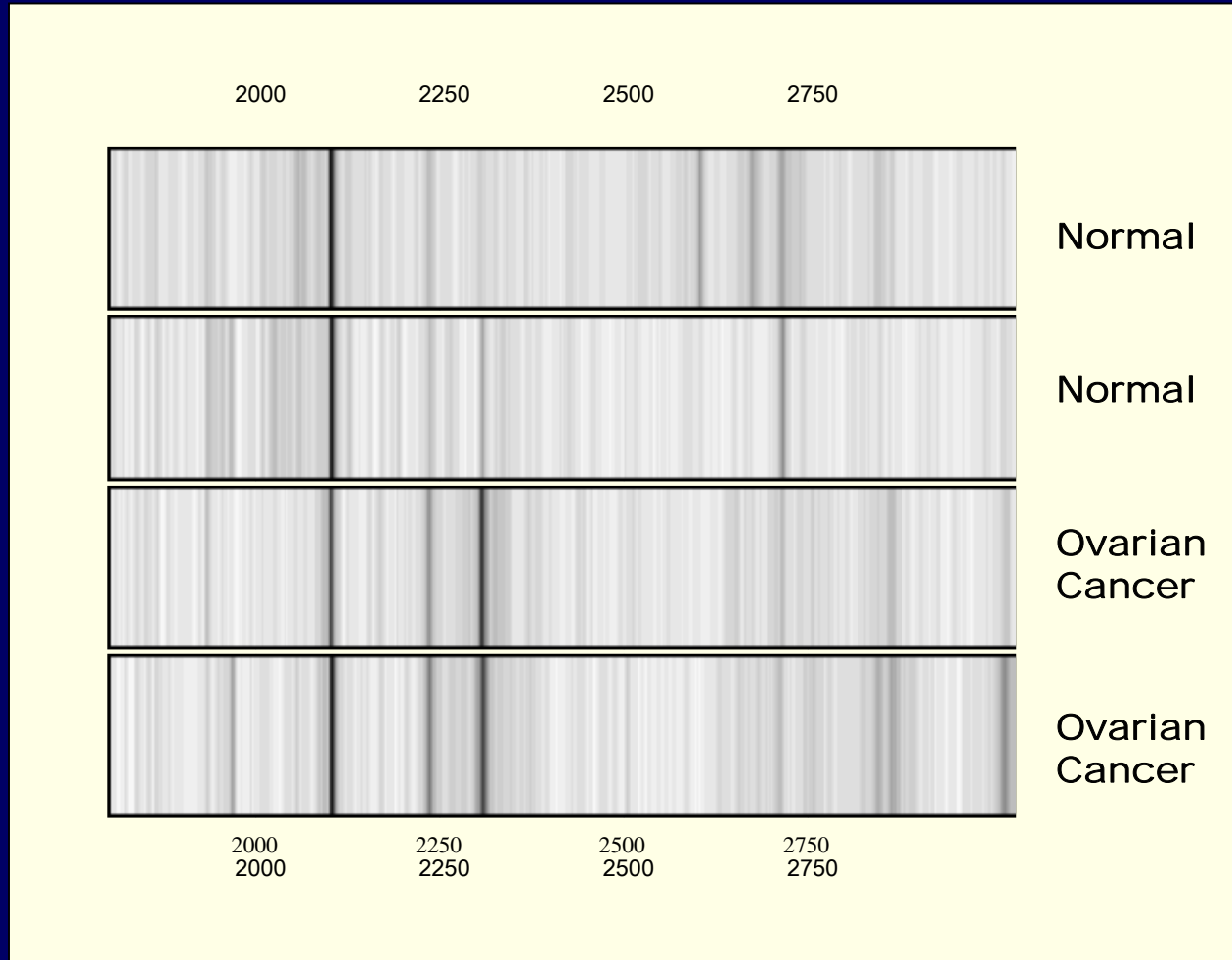
 AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE



GENE EXPRESSION ARRAY ANALYSIS



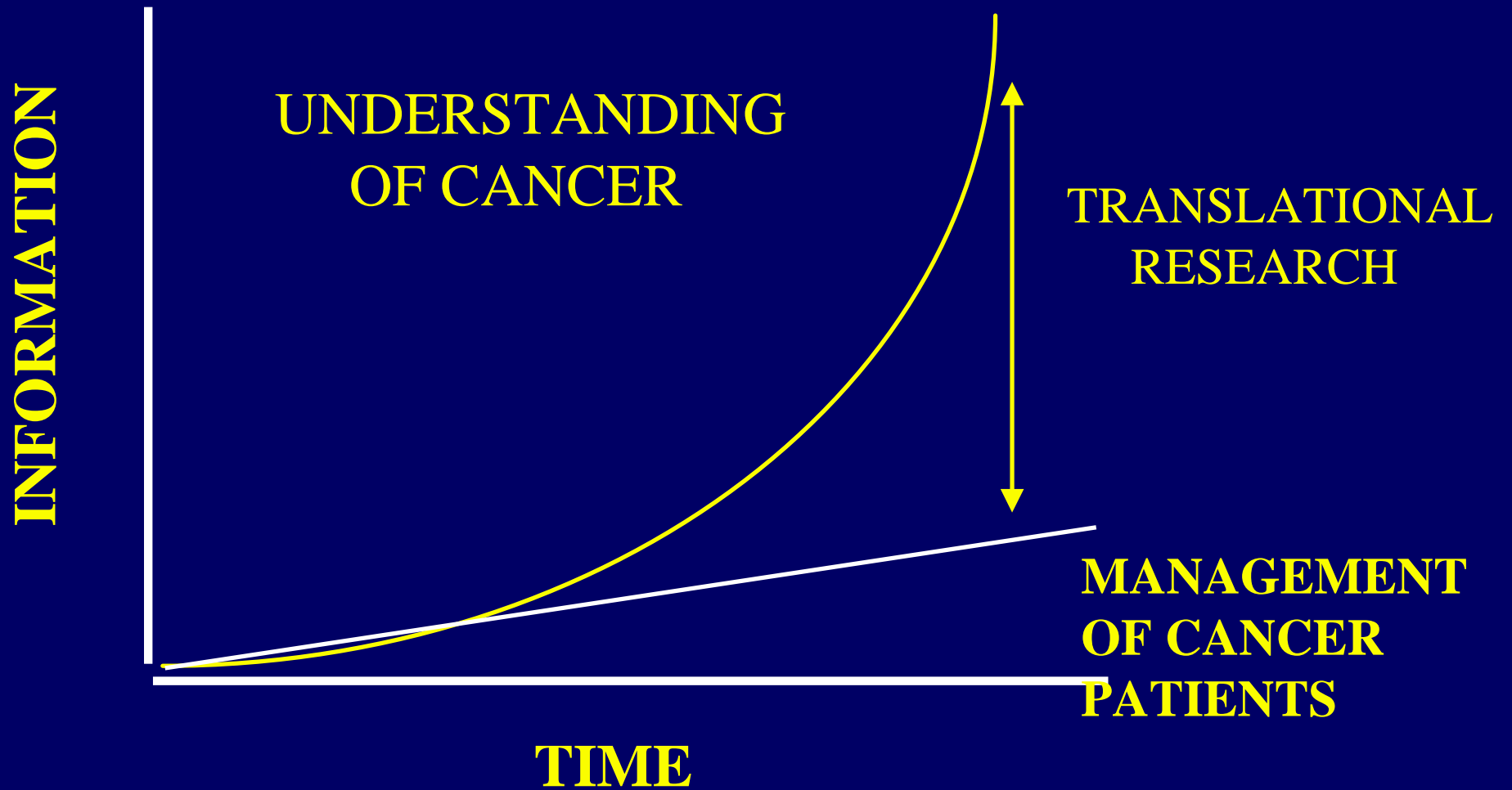
PROTEOMIC ANALYSIS



GROUNDS FOR OPTIMISM

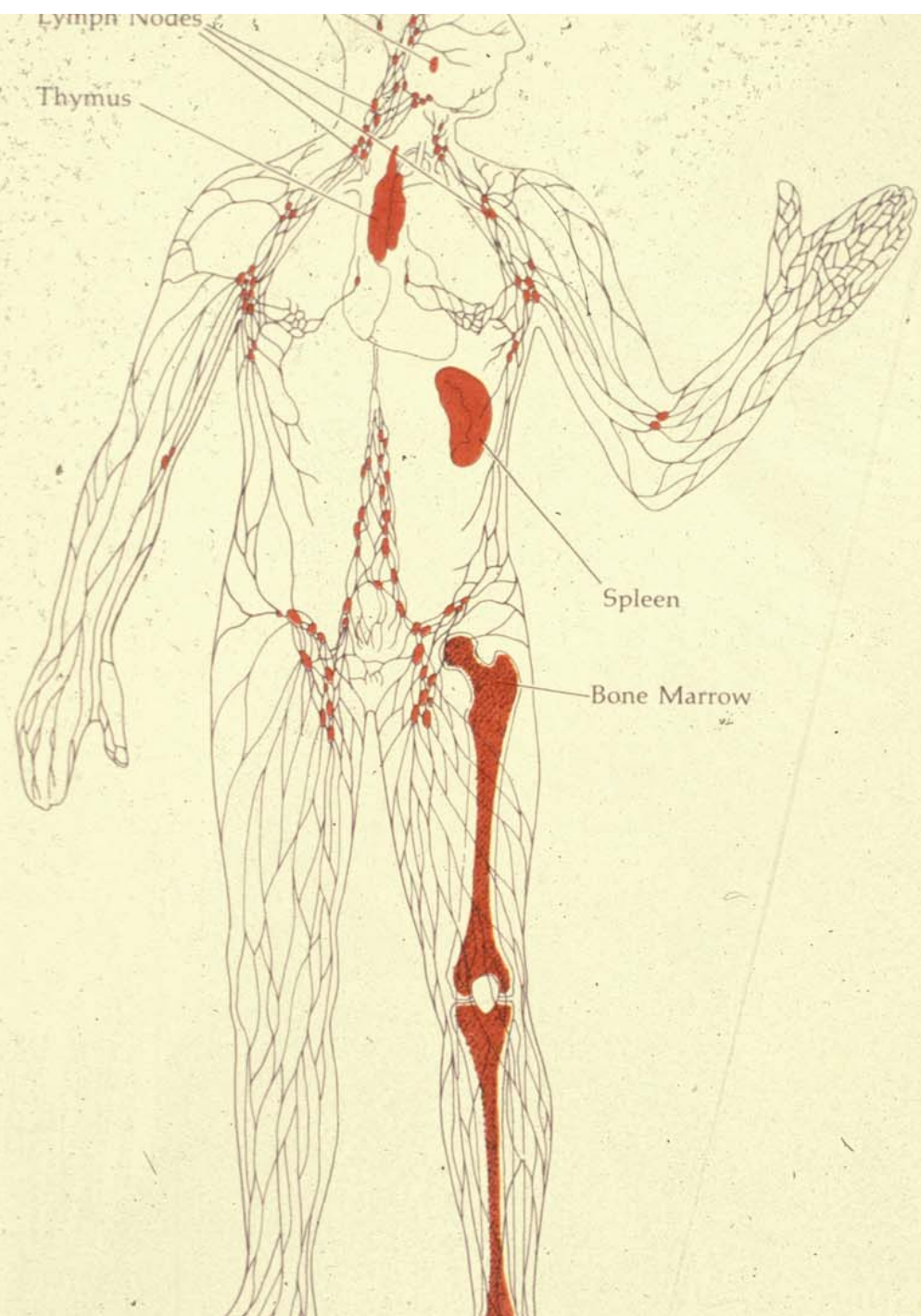
- **Omic Revolution**
- **Computer Revolution**
- **Informatic Revolution**

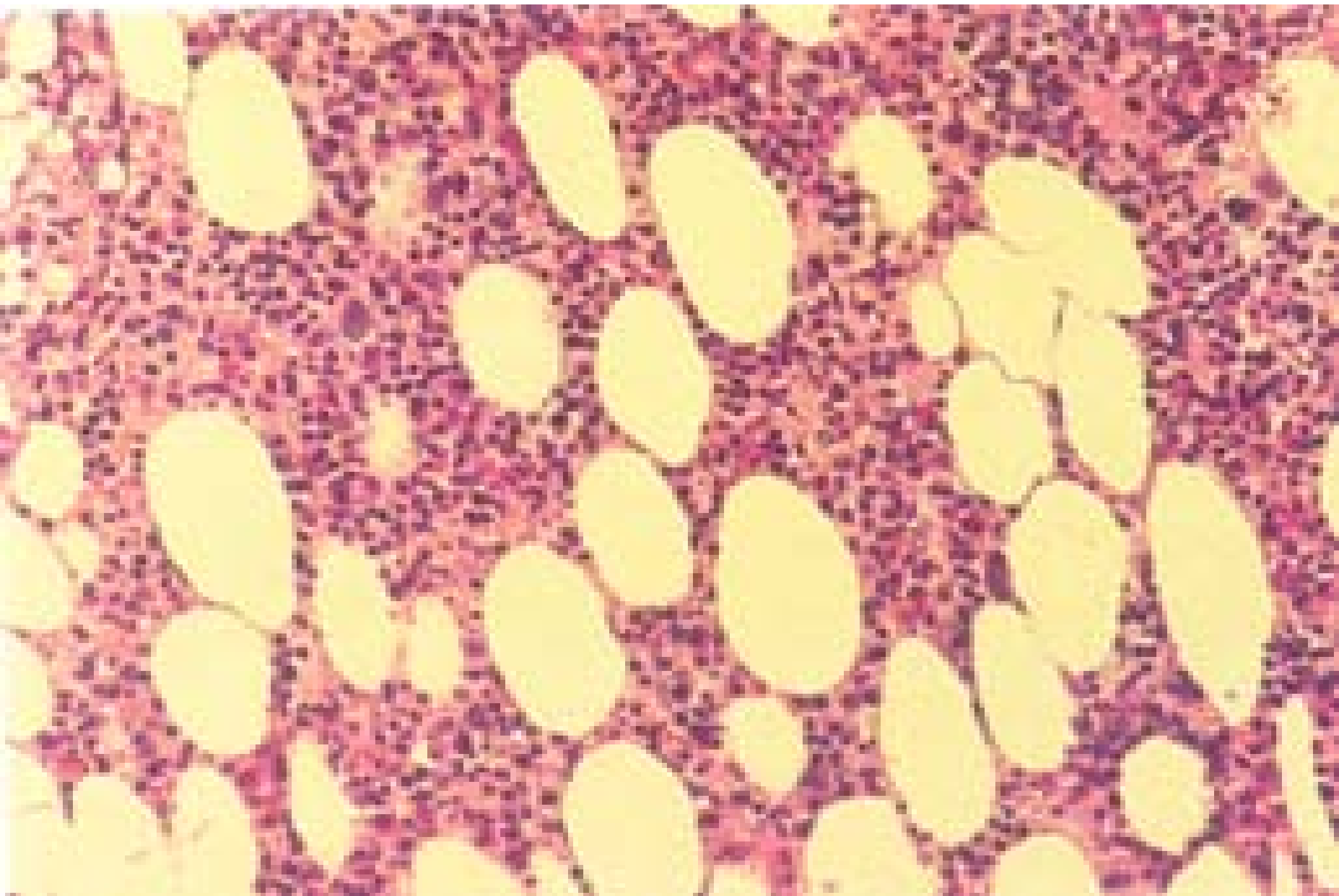
CHALLENGE FOR TRANSLATIONAL RESEARCH

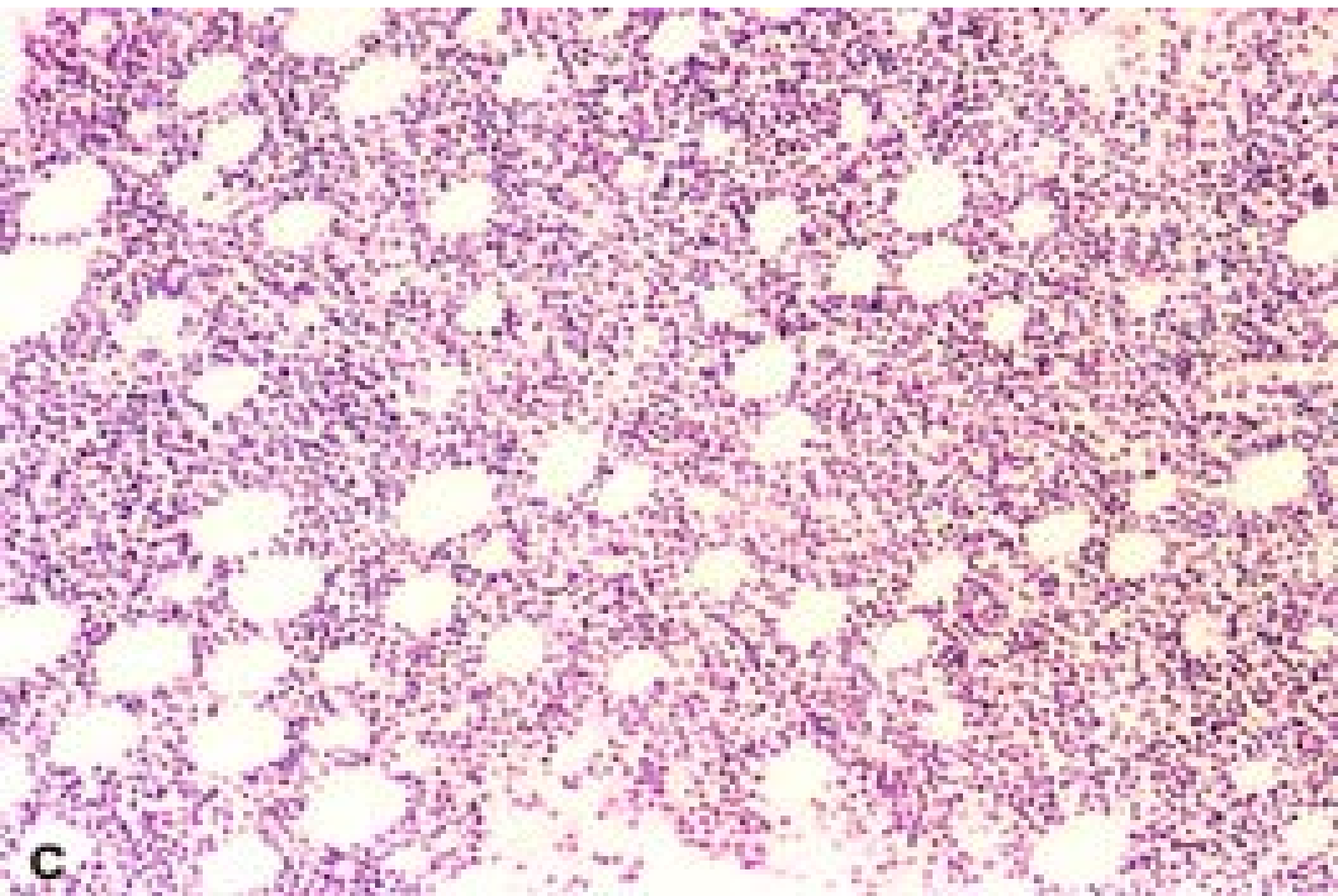


THE PROMISE OF MOLECULAR THERAPEUTICS

- By Studying the Alterations from Cancer to Cancer in DNA, RNA and Protein, we can Understand and Predict the Abnormal Behavior of Cancer Cells
- By Studying the Variations from Person to Person in Normal DNA, RNA and Protein we can understand and Predict the Toxic Effects of Cancer Treatment



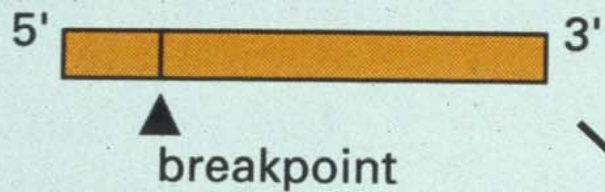




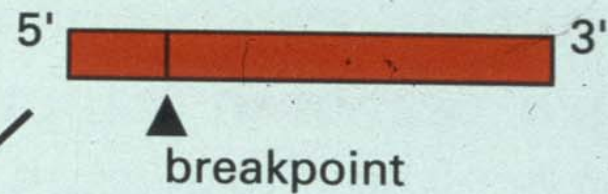
C



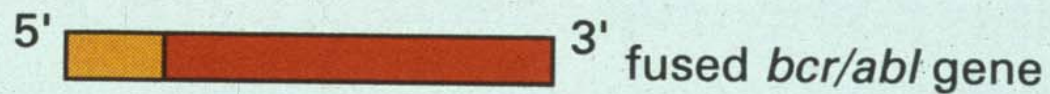
bcr gene on chromosome 22



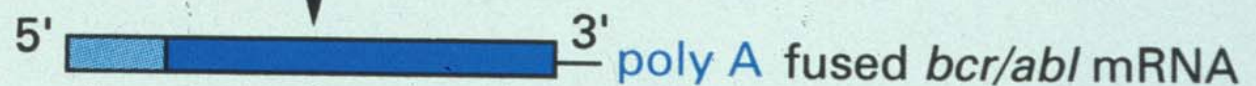
abl gene on chromosome 9



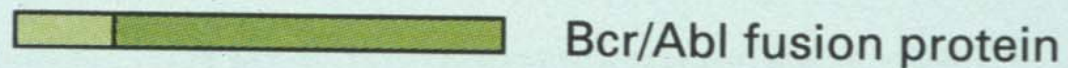
Ph' TRANSLOCATION



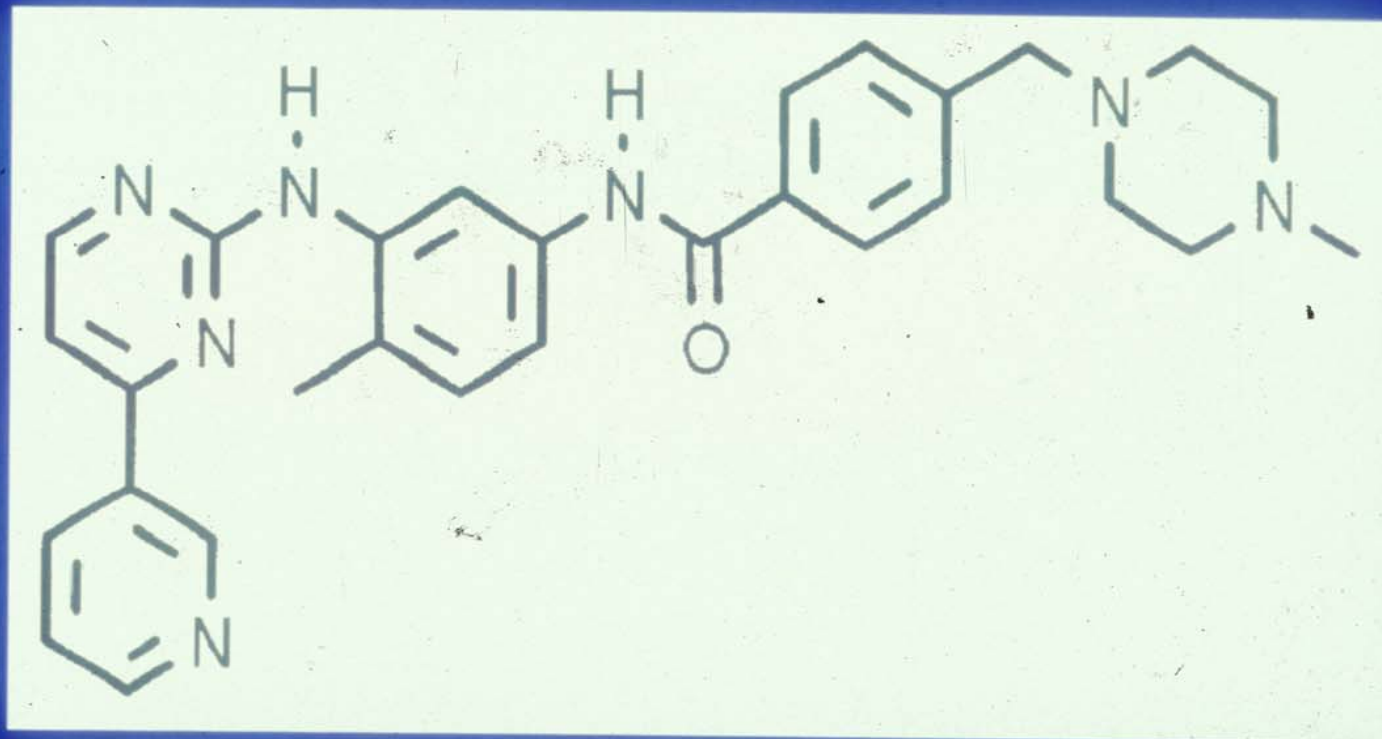
TRANSCRIPTION



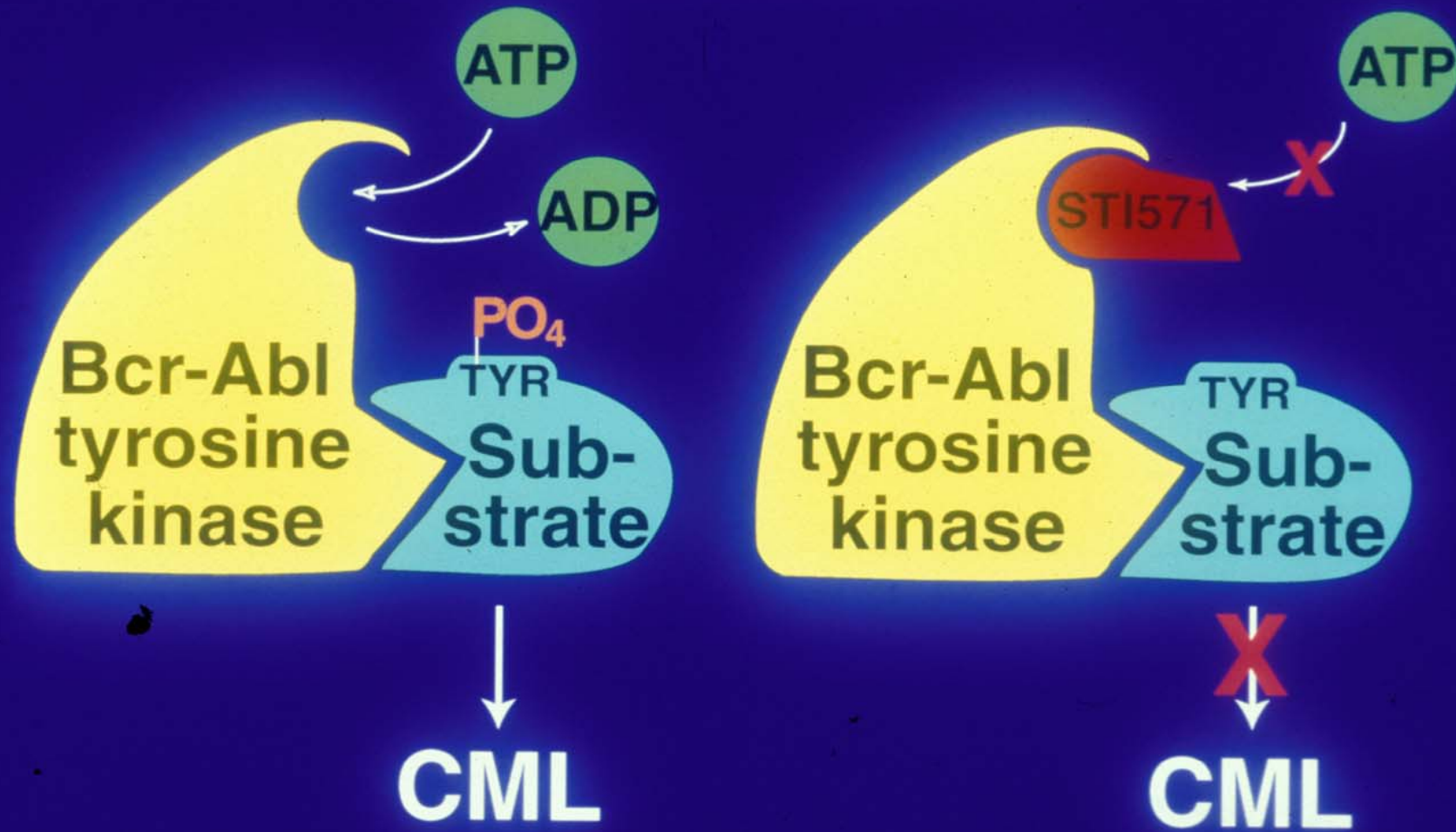
TRANSLATION



STI571
(CGP 57148B)
Glivec®



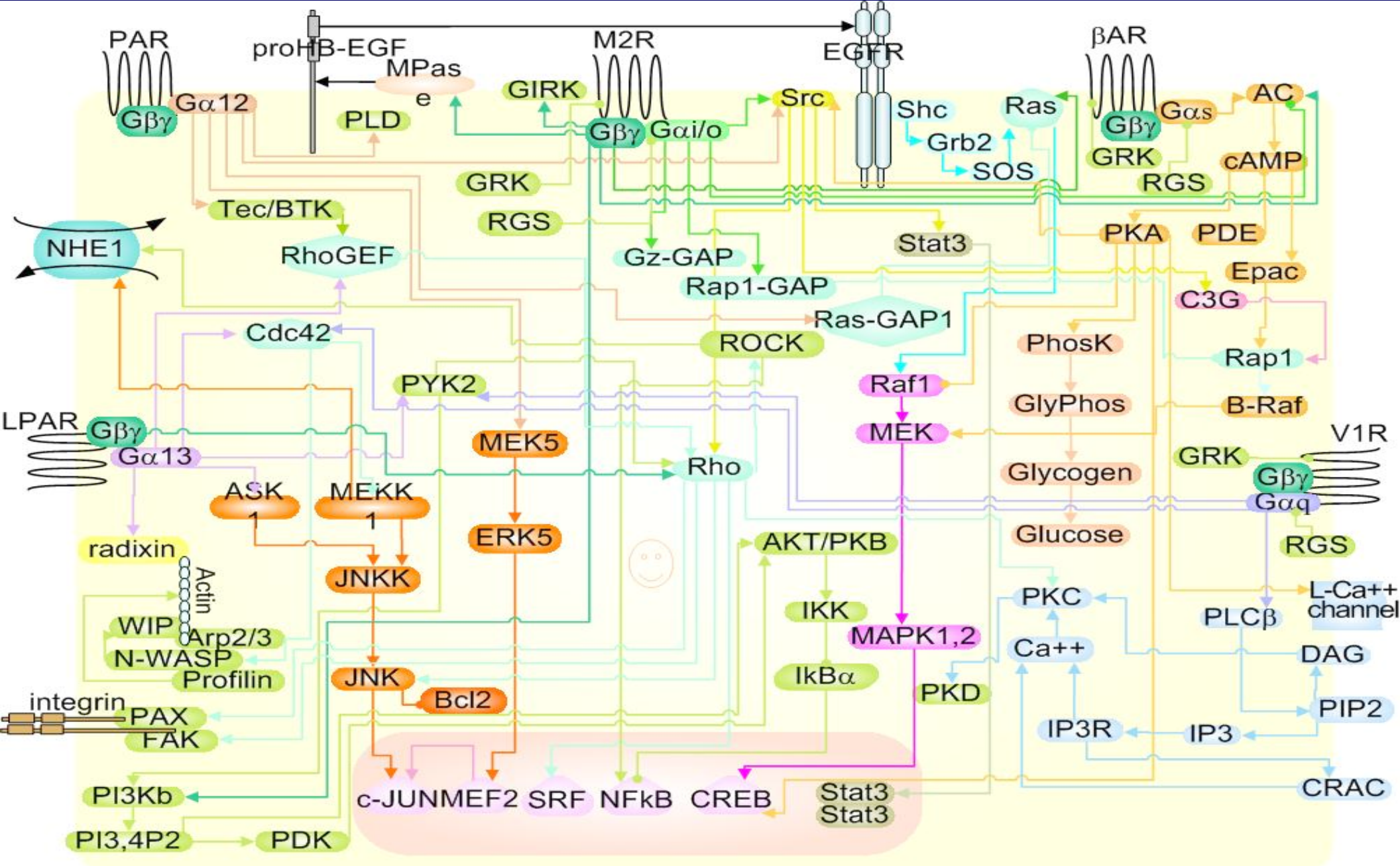
Bcr-Abl AS A THERAPEUTIC TARGET FOR CML



EFFICACY OF GLEEVEC IN CHRONIC MYELOGENOUS LEUKEMIA

	HEME RESPONSE	COMPLETE HEME RESPONSE	COMPLETE CYTOGENETIC RESPONSE
CHRONIC	98%	95%	28%
ACCELERATED	91%	44%	14%
BLAST CRISIS	64%	26%	6%

Intracellular signaling pathways



ELIMINATING CANCER IN THE 21st CENTURY

- **Bring Together Physicians, Scientists, Staff, Ideas, Drugs, Patients, Facilities, Informatics**
- **Establish a Creative Environment**
- **Work as a Team**
- **Collaborate Effectively with Government and Pharma**

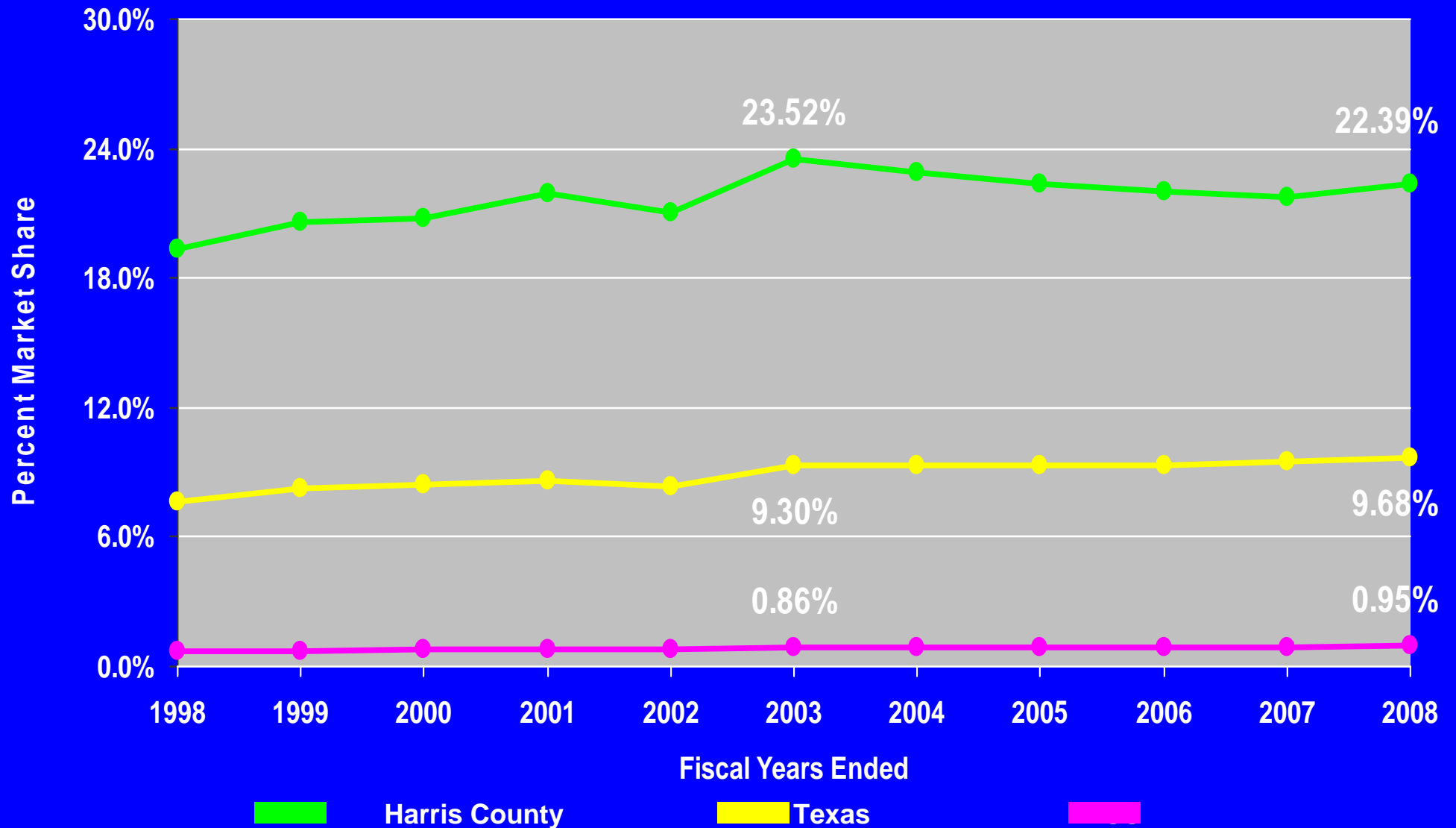
Why is M. D. Anderson the Leading Cancer Center Today?

- **Integrated free-standing center with a single mission**
- **1000 outstanding scientists and physicians**
- **Largest number of NCI grants and grant dollars for cancer research**
- **Research driven multidisciplinary care of 24,715 new cancer patients each year**
- **Largest Therapeutic clinical trial center in the country**

Patient Care Statistics

	<u>FY'03</u>	<u>5-Year % Growth</u>
Total Patients Served	66,241	38.8%
New Patients Served	24,411	38.0%
Admissions	19,430	22.0%
Surgeries	11,999	32.8%
Outpatient billable visits	537,822	45.9%
Radiation Procedures	252,583	80.7%
Lab Medicine Tests	6,029,953	53.9%
Diagnostic Imaging Studies	327,780	58.7%

UTMDACC Market Share – All Ages



Ambulatory Clinical Building

782,000 sf

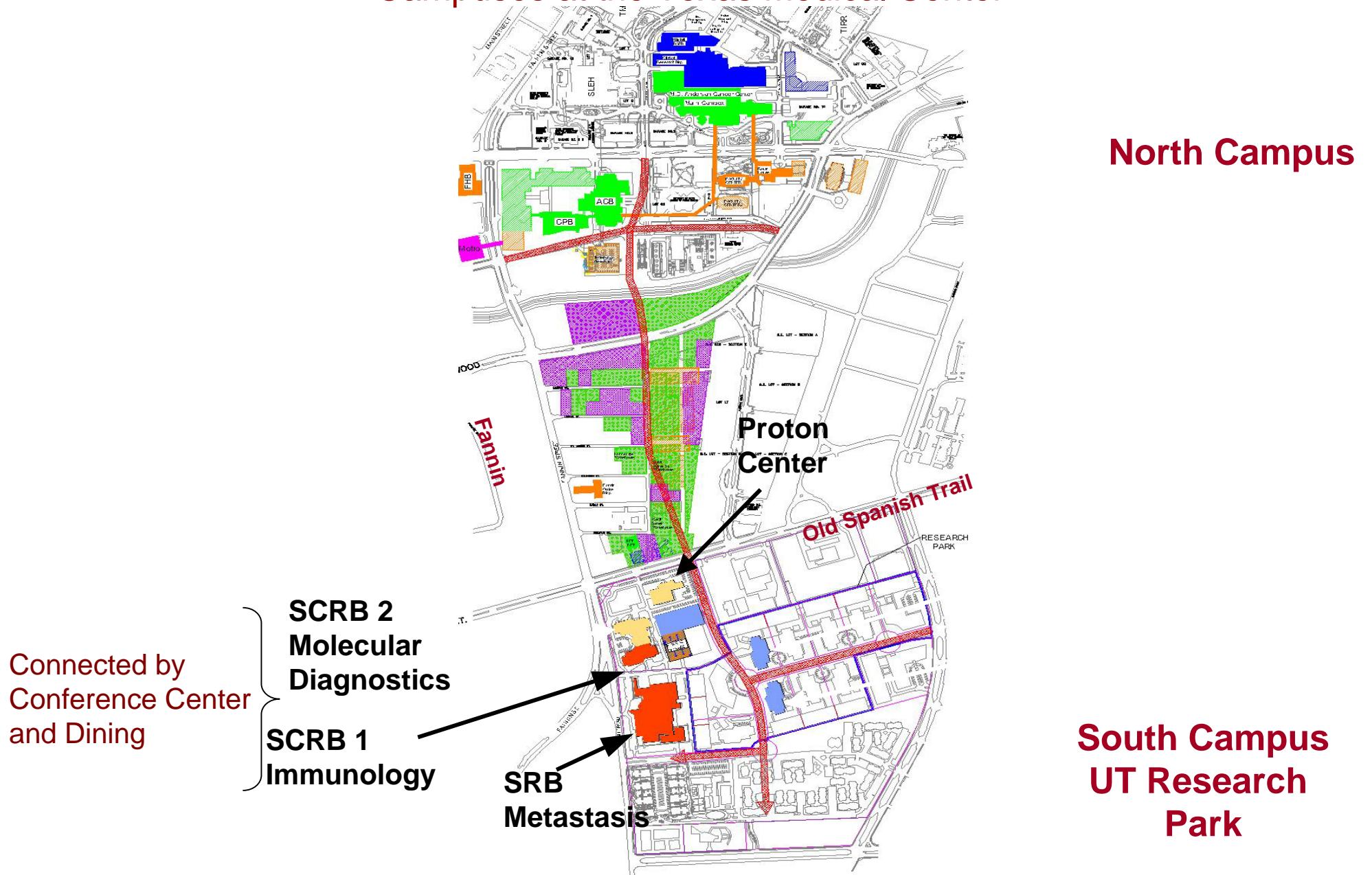


Research

	<u>2003</u>	<u>5 year % increase</u>
Research expenditures	\$282M	100%
Federal grant dollars*	\$164M	143%
No. peer-reviewed grants	510	67%
SPORES* (Specialized Programs of Research Excellence)	9	350%
Patients enrolled in therapeutic clinical trials	12,232	200%
Training grants	24	20%

***Most NCI grants (208), NCI grant dollars (\$98.4M) and SPORES of any academic institution**

The University of Texas M. D. Anderson Cancer Center Campuses at the Texas Medical Center



North Campus

Proton
Center

Old Spanish Trail

Connected by
Conference Center
and Dining

SCRIB 2
Molecular
Diagnostics

SCRIB 1
Immunology

SRB
Metastasis

South Campus
UT Research
Park

South Campus and UT Research Park



Emerging Research Theme #1: Molecular Diagnostics

- **Identify markers that detect cancer in an individual and predict response to treatment.**
 - **New Program in Molecular Markers**
 - **Genomics and Proteomics Core Laboratories**
 - **Annotated Tissue Banks**
 - **New Program in Molecular Imaging**

Early Detection of Ovarian Cancer

Ovaries

An anatomical diagram of the female reproductive system. The uterus is shown in the center, with fallopian tubes extending to the ovaries. The ovaries are highlighted in a bright red color, while the rest of the reproductive system is shown in shades of blue and purple. The diagram is set against a light purple background.

EARLY DIAGNOSIS

Ovarian Cancer Bar Code in Serum

PRINCIPLE

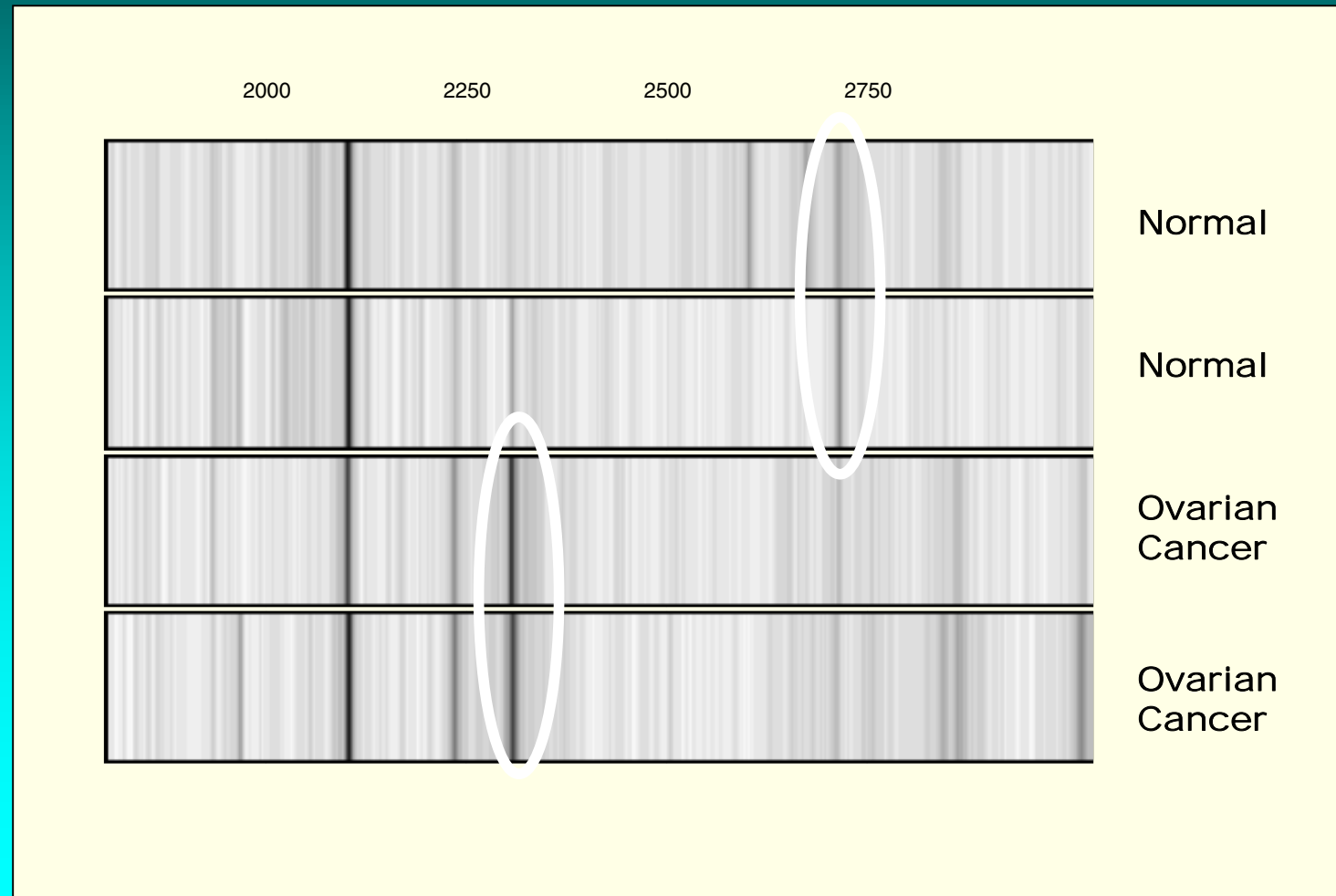
Analyze proteins

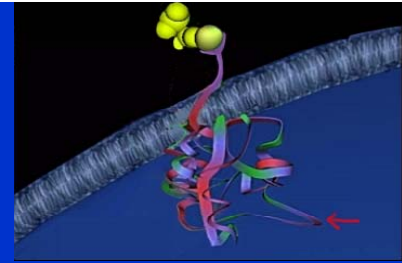
Patterns

400 controls

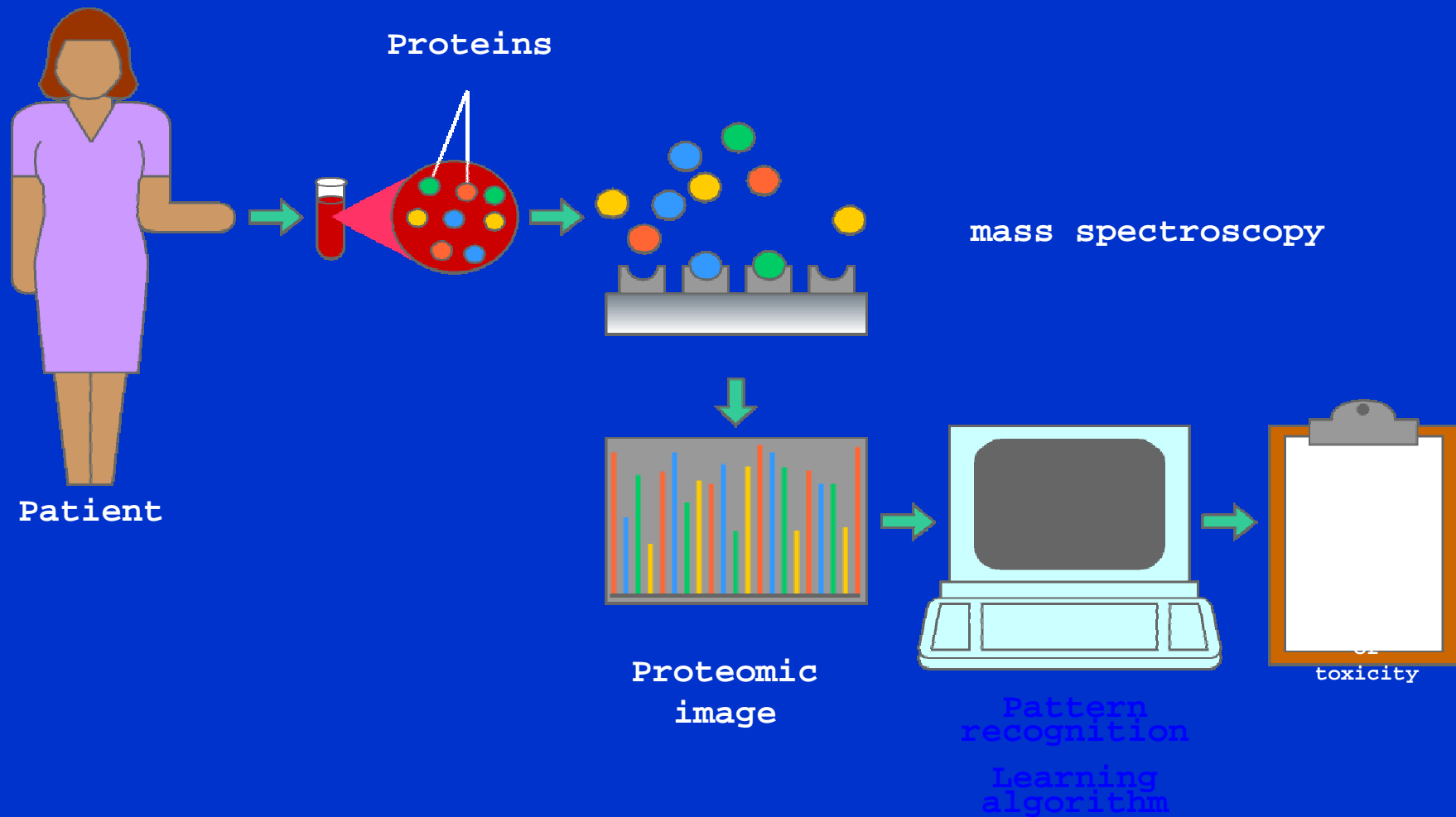
200 patients

OVER 95% OF
CANCERS DETECTED
AT CURABLE STAGE

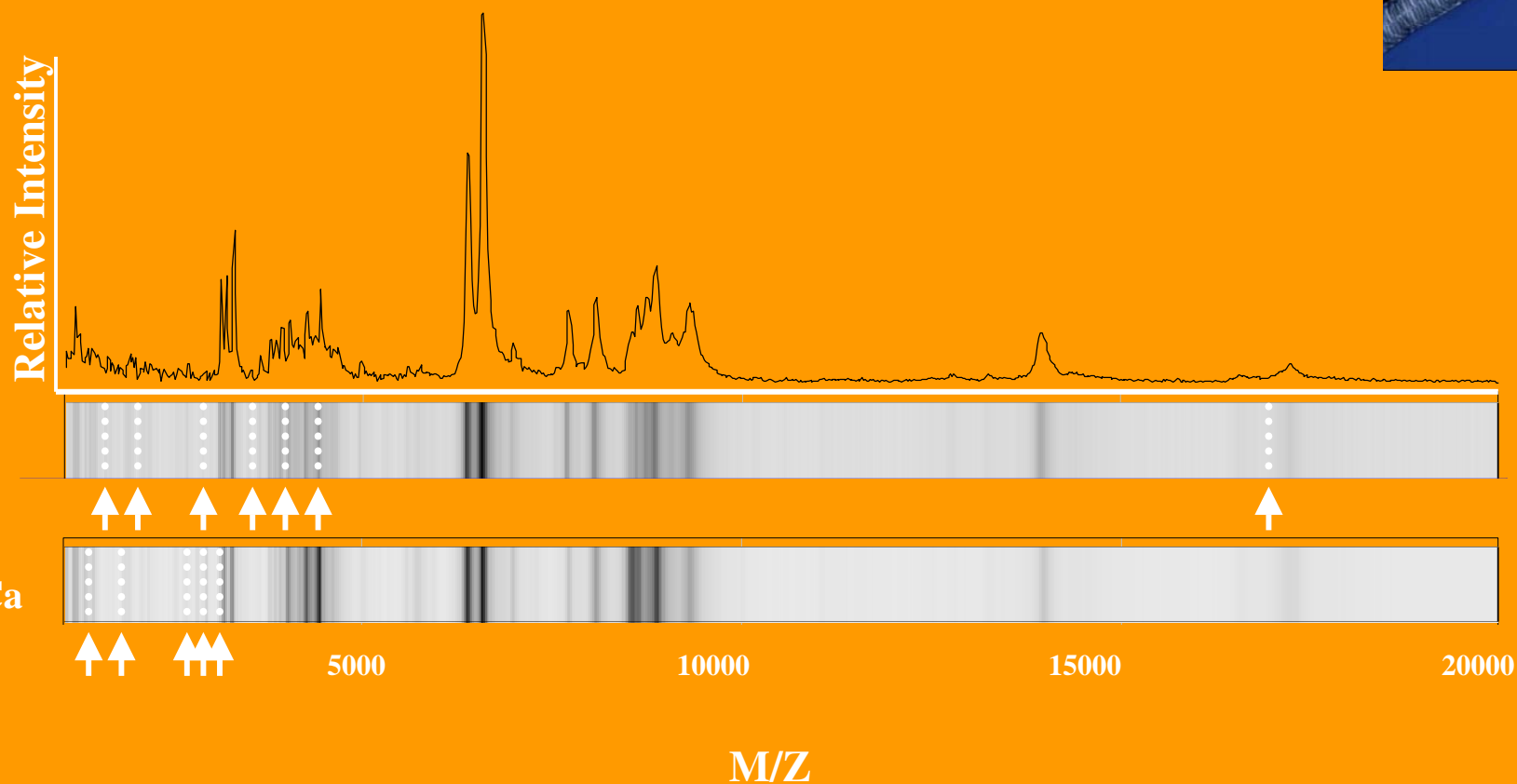
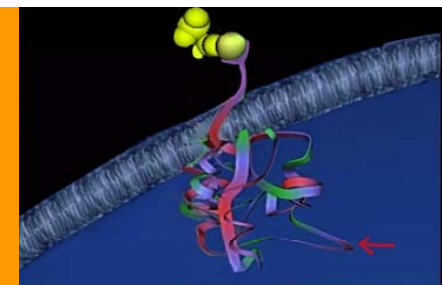




Serum Protein Pattern Diagnostics



Discovery of Diagnostic Signature Sets



IN PROGRESS

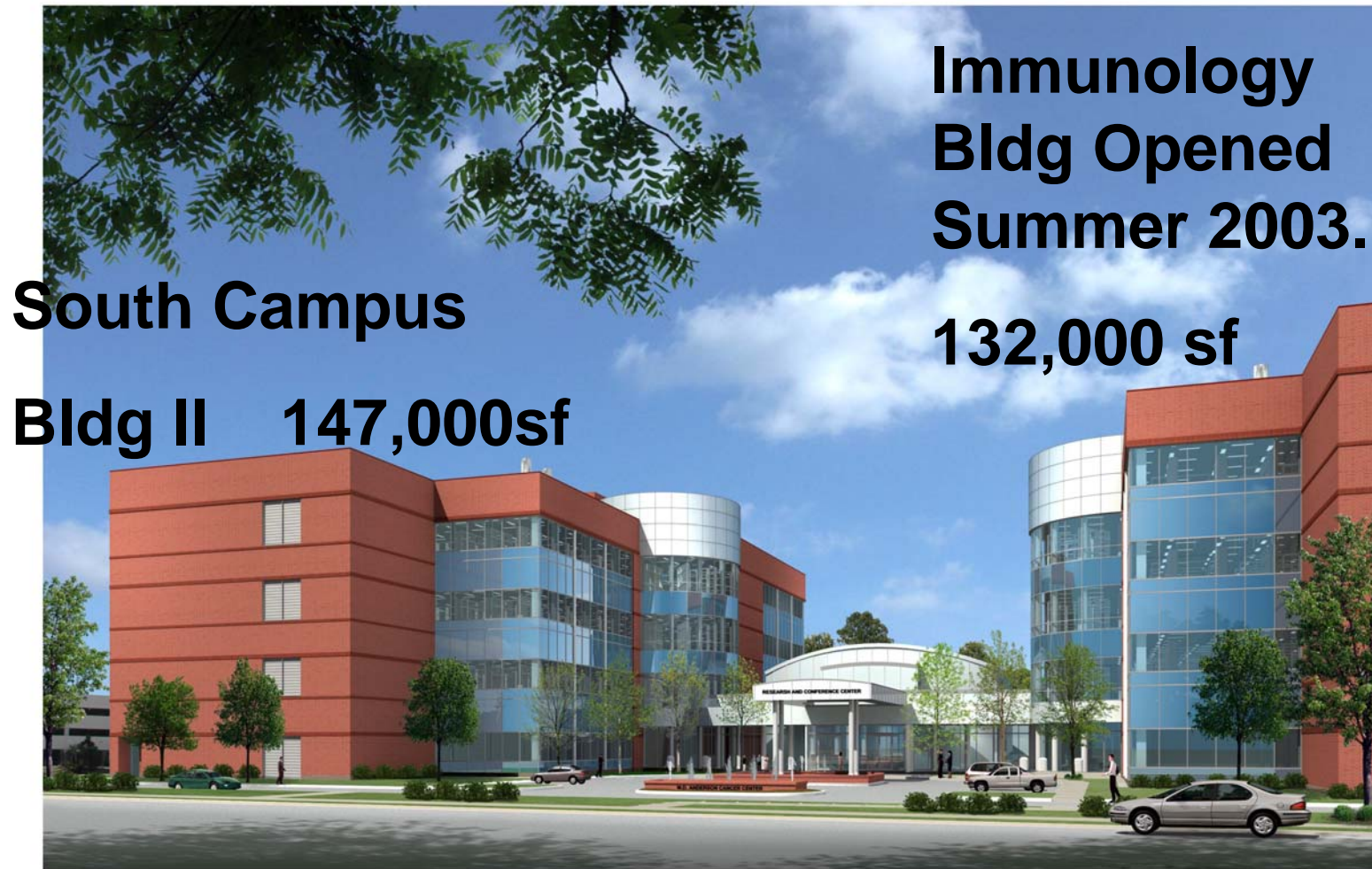
PROSTATE

OVARY

BREAST

LUNG

PANCREAS



**Immunology
Bldg Opened
Summer 2003.**

South Campus

132,000 sf

Bldg II 147,000sf

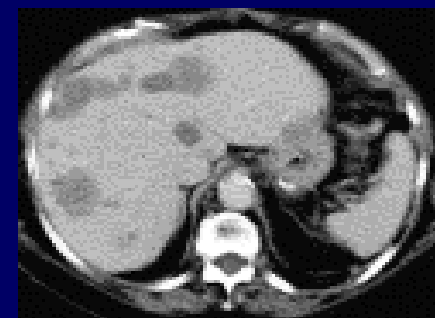
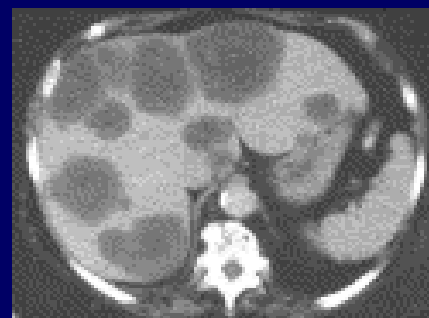
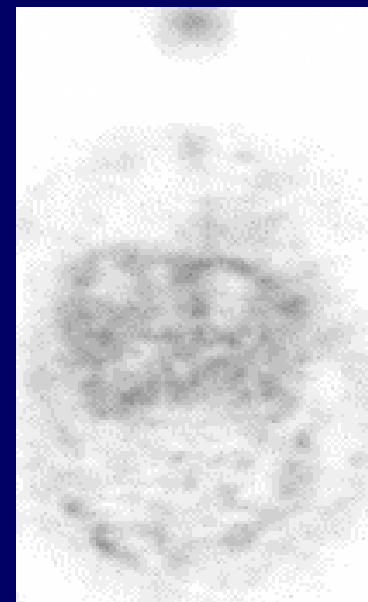
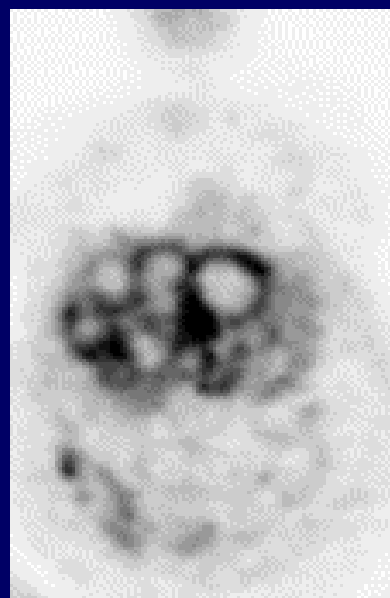
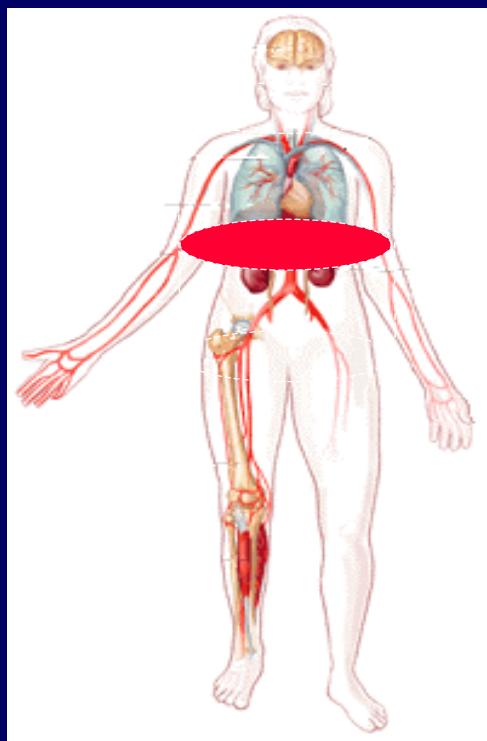
**The University of Texas M.D. Anderson Cancer Center
South Campus Research Buildings One and Two
and
Conference Center**

Molecular Imaging Research

- Direct Translation from Laboratory to Clinic
- Animal Imaging Facilities
- Diagnostic Imaging Center



**We can predict how well drugs will work by monitoring the function of their target (KIT and GIST)
Functional Imaging**



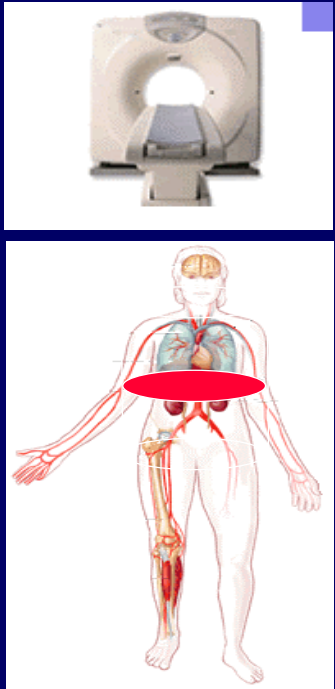
Before

8 days

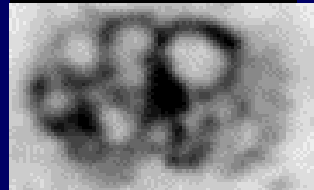
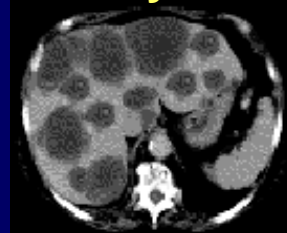
24 weeks

Future Diagnostic – Therapeutic Paradigm

PET/CTImaging



2-3 days



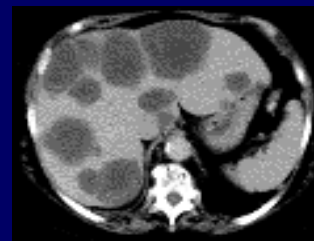
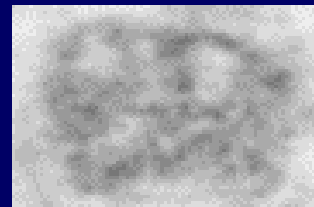
Therapy "A"

Therapy "B"

Therapy "A"

Therapy "B"

Therapy "B"



Center for Advanced Biomedical Imaging Research

South Campus Building III

- **Collaboration by UT MD Anderson, UT Health Science Center, General Electric Medical Systems and State of Texas**
- **PET scanning, MRI and other diagnostic imaging modalities**
- **Creation of Agents to image Genes, Proteins and Molecular Pathways; Radiochemistry to Label Reagents; Animal Imaging; Clinical Investigation in Patients**

Emerging Research Theme #2: Molecular Therapeutics

- **Develop new therapies targeting genes that cause cancer and molecular pathways that promote cancer cell proliferation, survival and metastasis.**
 - **Clinical and Translational Research Center**
 - **Pharmaceutical Development Center**
 - **Animal Toxicology/GLP Facility**
 - **Molecular Monitoring Laboratory**
 - **Re-engineering of Technology Transfer**
 - **Strategic Alliances with Pharma**

MDACC-Pharma Collaborations

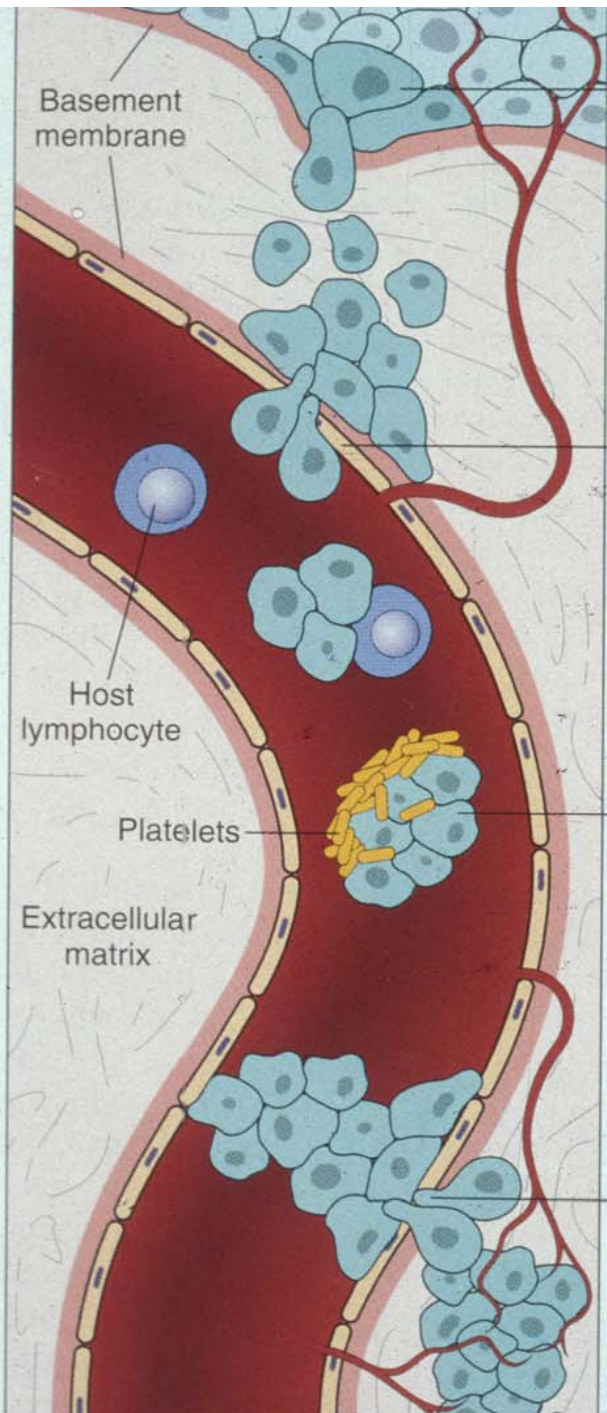
- **Speed New Drug Development**
- **Pre-clinical as well as Clinical Research**
- **Validate “Targets”**
- **Develop Molecular Diagnostics**
- **Design “Intelligent Trials” with Biological Endpoints**
- **Identify Biomarkers for Response to Individualize Treatment**

South Campus and UT Research Park



Emerging Research Theme #3: Microenvironment of Cancer

- **Understand the critical role of surrounding normal tissues in promoting cancer growth, e.g., blood vessels, growth factors.**
 - **Metastasis Center**
 - **Targeting normal tissue**
 - **Anti-vascular Therapy**



Metastatic subclone

Adhesion to and invasion of basement membrane

Passage through extracellular matrix

Intravasation

Interaction with host lymphoid cells

Tumor cell embolus

Adhesion to basement membrane

Extravasation

Metastatic deposit

Basement membrane

Host lymphocyte

Platelets

Extracellular matrix

Smith Research Building



Emerging Research Theme #4: Immunotherapy

- **Create new immunological approaches to the treatment of cancer**
- **Characterize the cells, antibodies and cytokines involved.**
 - **New Chairs of Immunology, Melanoma and Lymphoma/Myeloma**
 - **New Center for Cancer Immunology Research**
 - **GMP facility for stem cell and immunotherapy**

Center for Cancer Immunology Research South Campus Research Building I

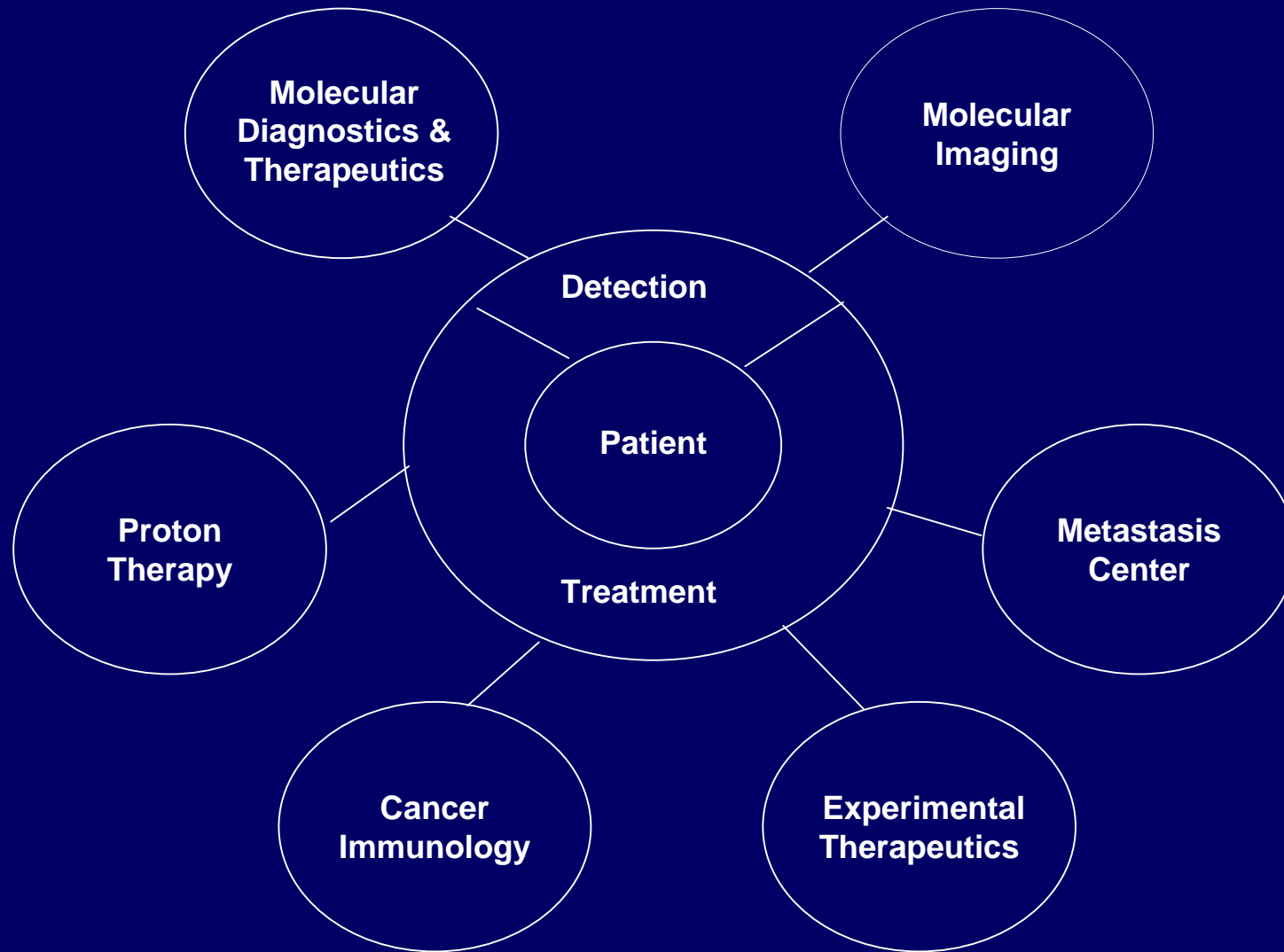


Proton Therapy Center

85,000 sf



South Campus Initiative

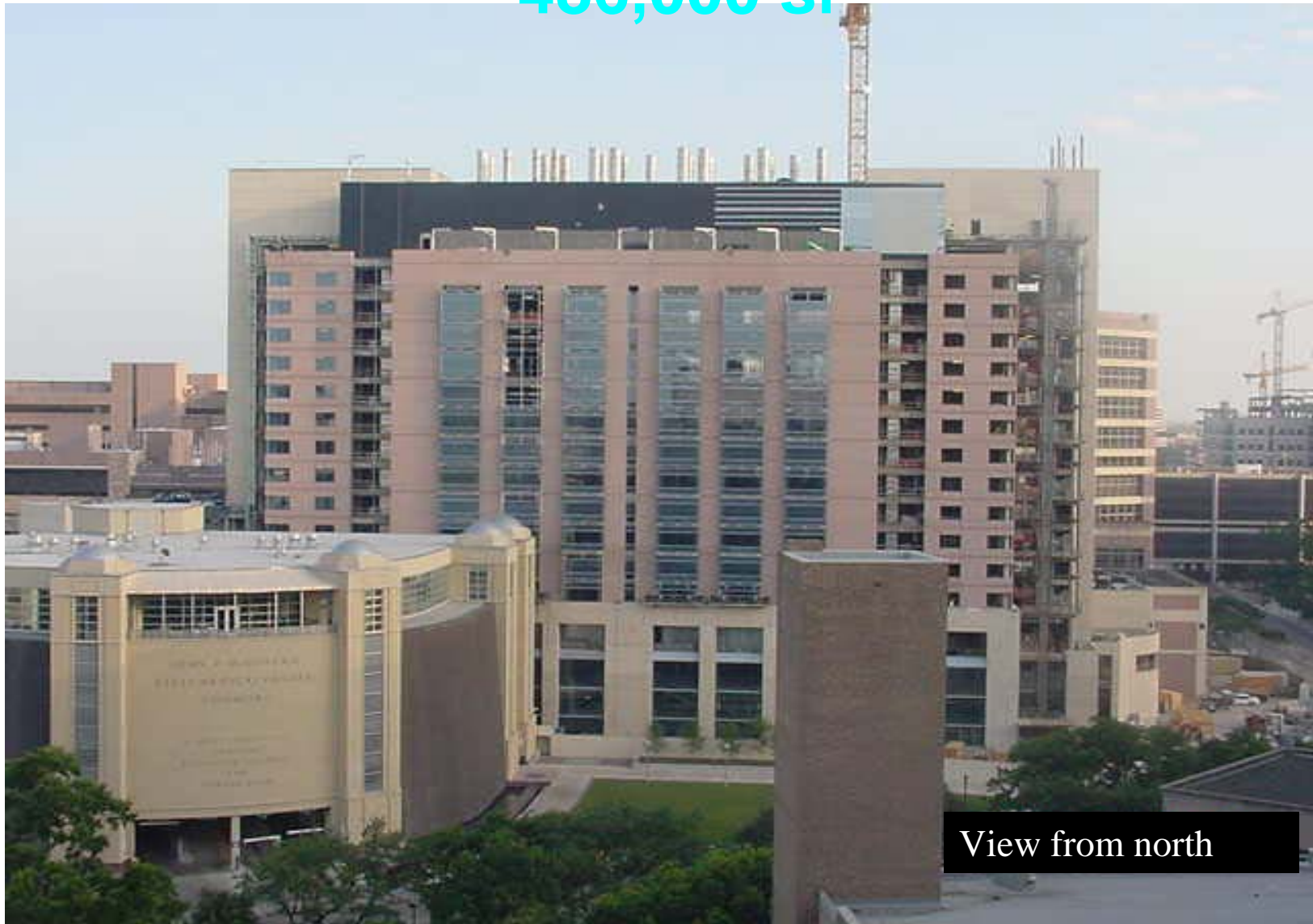


Emerging Research Theme #5: Stem Cell Research

- **Function and Definition of Blood and Cancer Stem Cells**
 - **Largest blood and marrow stem cell clinical program.**
 - **GSBS Program in Genes and Development**
 - **Genetically-engineered mouse models**
 - **Research on DNA/chromatin modification and regulation of transcription.**

George and Cynthia Mitchell BSRB

486,000 sf



View from north

Emerging Research Theme #6: Cancer Prevention

- **Identify genetic, environmental and lifestyle factors that determine cancer risk**
- **Find therapeutic agents and behavioral modifications that can prevent cancer or reverse precancerous conditions.**
 - **Division of Cancer Prevention: 10th year**
 - **Smoking prevention programs**
 - **New Department of Health Disparities Research**
 - **Mexican American Cohort Study**
 - **Chemoprevention clinical trials**

Cancer Prevention Building

391,000 sf



ACB

01/05/2004

Emerging Research Theme #7: Organ Site Research

- **Understand cancer that starts in Different Organs, Exploring new Diagnostic and Therapeutic Approaches**
 - **Promote collaborative research and grant support targeting specific cancers.**
 - **9 SPOREs (Specialized Program of Research Excellence)**
 - **Establish priorities to accept patients for whom we can provide unique care or innovative clinical trials**
 - **Explore differences in pediatric and adult cancers.**
 - **Expand National and International Collaborations**

ELIMINATING CANCER IN THE 21st CENTURY

- **Analyze Enormous Amounts of Complex Data**
- **Link Laboratory Data with Clinical Outcomes**
- **Develop Reliable Models that Predict the Behavior of Networks**
- **Develop Team Science**

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

Making Cancer History[®]