BIOE 301

Lecture Fifteen

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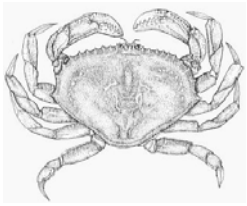
Office Hours: Mon 1-4 PM

Bioengineering and Prostate Cancer



- Risk factors
- Detection
- Treatment
- New technologies
- Challenges

Challenge: Should we screen?

- Costs
- Efficacy of screening

DRE/PSA test	$30-100
Prostate biopsy	$700-1500

Cost of screening

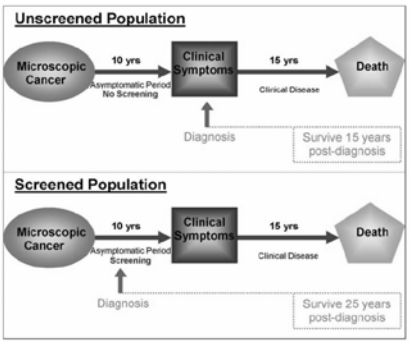
- Screening Performance:
  - Se = 73%; Sp = 90%
- Number Tested:
  - N=1,000,000; Prevalence = 2%
- Costs:
  - Screening = $30; Follow up biopsy = $1500
- What is detection cost?
- What is cost/cancer found?

	Test Positive	Test Negative	
Disease Present	14,600	5,400	# with Disease = 20,000
Disease Absent	98,000	882,000	#without Disease = 980,000
	# Test Pos = 112,600	# Test Neg = 887,400	Total Tested = 1,000,000

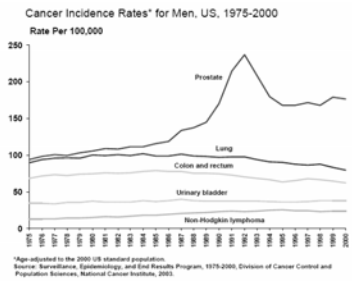
Cost to Detect =$30*1,000,000+$1500*112,600 =$168,900,000
Cost/Cancer = $168,900,000/14,600=$13,623

Efficacy of screening

- DRE Case studies
  - Mixed results
- PSA test
  - Mortality decreased 42% since 1993 in Tyrol, Austria
- RCT's
  - ERSPC
  - PLCO



Why are RCTs so Important?
Lead Time Bias



	5-Year Survival, %			% Change (1950-1996)	
	1950-1954	1989-1995	Absolute Increase in 5-Year Survival, %	Mortality	Incidence
Prostate	43%	93%	50%	+10%	+190%
Cervix	59%	71%	12%	-76%	-79%
Ovary	30%	50%	20%	-2%	+3%

Should we screen?

- Yes:
  - Localized prostate cancer is curable
  - Advanced prostate cancer is fatal
  - Some studies (not RCTs) show decreased mortality in screened patients
- No:
  - False-positives lead to unnecessary biopsies
  - Over-detection of latent cancers
    - We will detect many cancers that may never have produced symptoms before patients died of other causes (slow growing cancer of old age)
  - No RCTs showing decreased mortality

Screening guidelines

Organization	Recommendation
American Academy of Family Medicine	Physicians should counsel men between ages of 50 and 65 about known risks and uncertain benefits of screening so they may make an informed choice.
American Cancer Society	Offer the PSA and DRE tests annually beginning at age 50 to men who have a 10 year life expectancy and to younger men at higher risk
American College of Physicians	Physicians should describe potential benefits and known harms of screening, diagnosis an treatment, listen to patient's concerns and individualize the decision of whether to screen
American Urological Association	Men over 5 should consider testing. Men at high risk should begin testing at age 45.
CDC	Routine screening is not recommended because there is not consensus on whether screening and early treatment reduces mortality.
US Preventive Services Task Force	Evidence is insufficient to determine whether the benefits of screening outweigh the harms.

Do All Countries Screen with PSA?

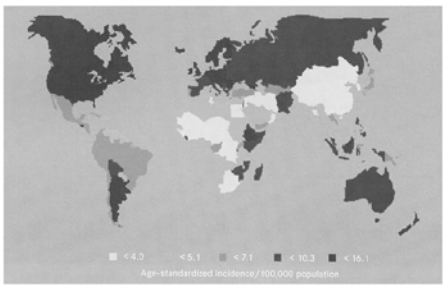
- United States:
  - Conflicting recommendations
- Europe:
  - No
  - Not enough evidence that screening reduces mortality

Bioengineering and Ovarian Cancer

Statistics on Ovarian Cancer

- United States:
  - Incidence: 22,430
  - Mortality: 15,280
- Worldwide:
  - Incidence: 190,000
  - Mortality: 114,000

Global Burden of Ovarian Cancer

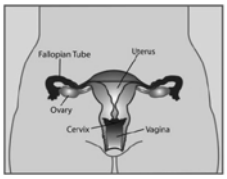


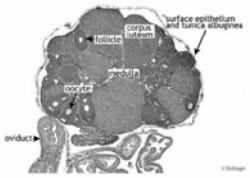
Risk factors

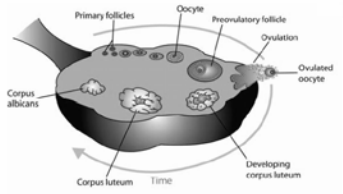
- Age
  - Most ovarian cancers develop after menopause
- Personal or family history of breast, ovarian, endometrial, prostate or colon cancer.
- Reproductive history

  Increases with the more lifetime cycles of ovulation that a woman has undergone. Thus, women who have undergone hormonal treatment for infertility, never used birth control pills, and who never became pregnant are at higher risk for ovarian cancer

Pathophysiology



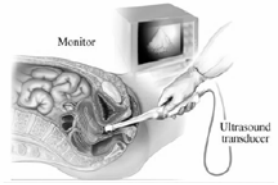


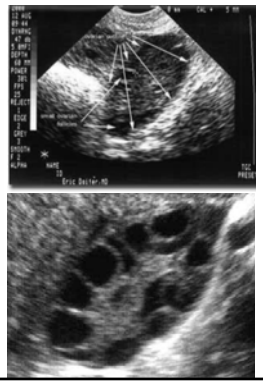


Screening of Ovarian Cancer

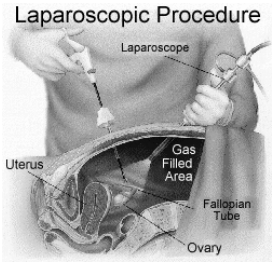
- Pelvic and rectal exam
- CA125 test
- Transvaginal sonography

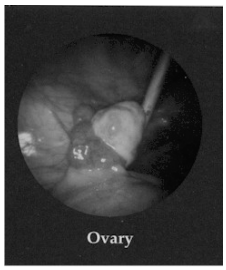
Transvaginal Sonography





Diagnostic Laparoscopy





Complication Rate = 0.5 – 1%

Detection and Treatment

- Screening
  - Pelvic exam
  - CA125 test
  - Transvaginal ultrasound
- Diagnosis
  - Diagnostic laparoscopy
- Treatment:
  - Surgery, radiation therapy, chemotherapy
- 5 year survival
  - Localized disease: 93% (20% diagnosed at this stage)

Screening Scenarios

- Scenario #1:
  - Screen 1,000,000 women with CA125
    - p = .0001 (100 cancers)
    - Se=35%, Sp=98.5%
    - Cost = $30
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=$2,000
- TP=35 FP=14,999 Complications=150
- PPV =0.23% NPV =99.99%
- Cost per cancer found = $1,716,200

Screening Scenarios

- Scenario #2:
  - Screen 1,000,000 women with transvaginal US
    - P = .0001 (100 cancers)
    - Se=100%, Sp=96%
    - Cost = $150
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=$2,000
- TP=100 FP=39,996 Complications=401
- PPV =0.25% NPV =100%
- Cost per cancer found = $300,672

Screening Scenarios

- Scenario #3:
  - Screen 1,000,000 women >age 50 with TVUS
    - P = .0005 (500 cancers)
    - Se=100%, Sp=96%
    - Cost = $150
  - Follow with laparoscopy
    - Complication rate = 1%
    - Cost=$2,000
- TP=500 FP=39,980 Complications=405
- PPV =1.24% NPV =100%
- Cost per cancer found = $60,670

Screening Scenarios

- Scenario #3 cont.:
  - Screen 1,000,000 women > age 50 with TVUS
    - P = .0005 (500 cancers)
    - Se=100%, Sp=??%
    - Cost = $150
  - How high does Sp need to be for PPV to reach 25%?
    - Sp = 99.985%

Does Ultrasound Screening Work?

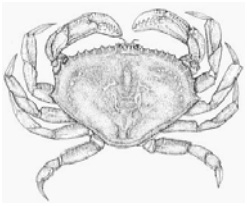
- Two studies of over 10,000 low-risk women:
  - The positive predictive value was only 2.6%
  - Ultrasound screening of 100,000 women over age 45 would:
    - Detect 40 cases of ovarian cancer,
    - Result in 5,398 false positives
    - Result in over 160 complications from diagnostic laparoscopy
  - Jacobs I. Screening for early ovarian cancer. Lancet; 2:171-172, 1988.

Ongoing Clinical Trials

- United Kingdom
  - 200,000 postmenopausal women
    - CA 125 level plus transvaginal ultrasound examination
    - Transvaginal ultrasound alone
    - No screening
- United States:
  - 37,000 women (aged 55–74)
    - Annual CA 125 level and transvaginal ultrasound examination
    - No screening
- Europe:
  - 120,000 postmenopausal women
    - No screening,
    - Transvaginal ultrasound at intervals of 18 months
    - Transvaginal ultrasound at intervals of 3 years

http://www.mja.com.au/public/issues/178_12_160603/and10666_fm.pdf

Ovarian Cancer



Risk factors
Detection
Treatment
Challenges
New technologies

Challenge

Better screening methods to detect early stages of ovarian cancer

Cancer Screening Exams

- Cellular/Morphological Markers
  - Pap smear
- Serum protein markers
  - PSA
  - CA125
- DNA markers
  - HPV DNA

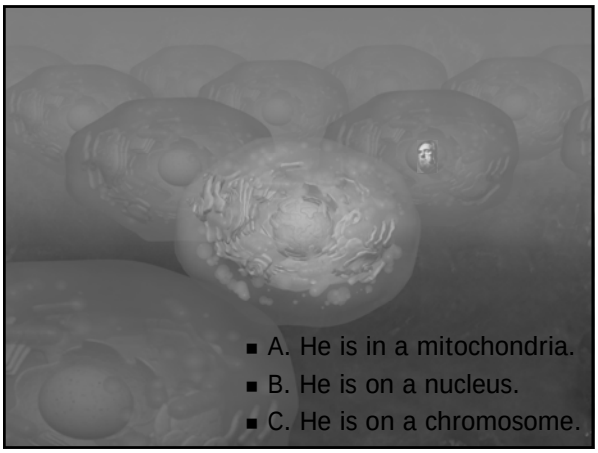
How do we choose a target?

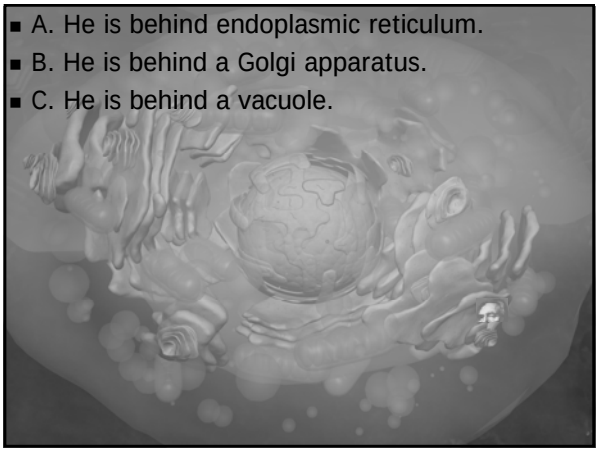
Lets play...

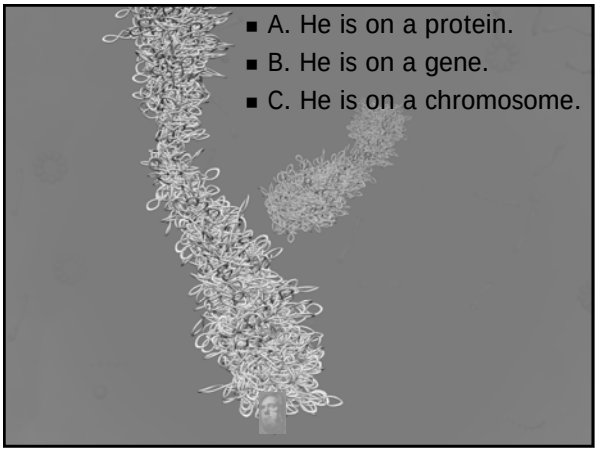
Where in the World is C. Everett Koop?

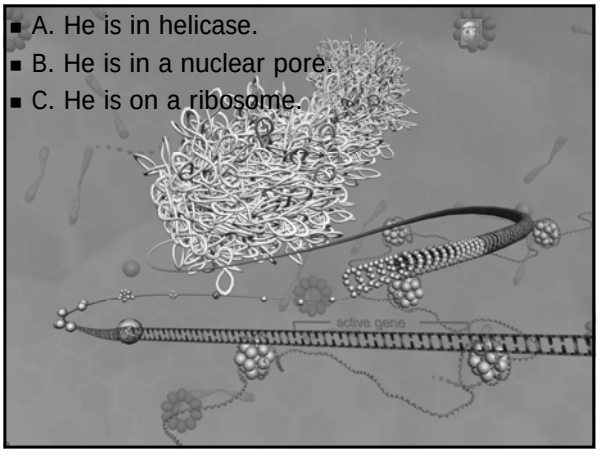
Here's how to play:

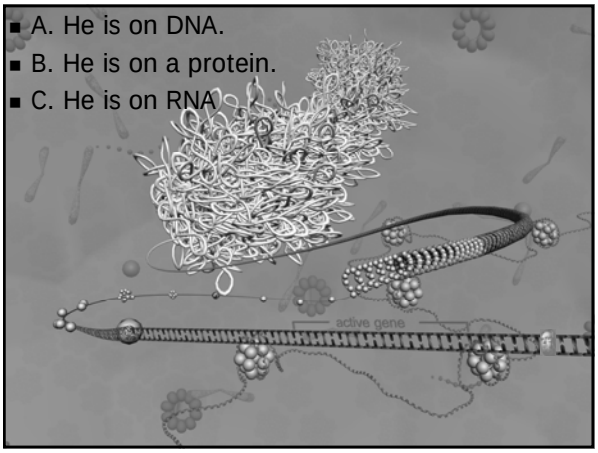
- Take a good look at each of the following pictures and try to spot C. Everett Koop.



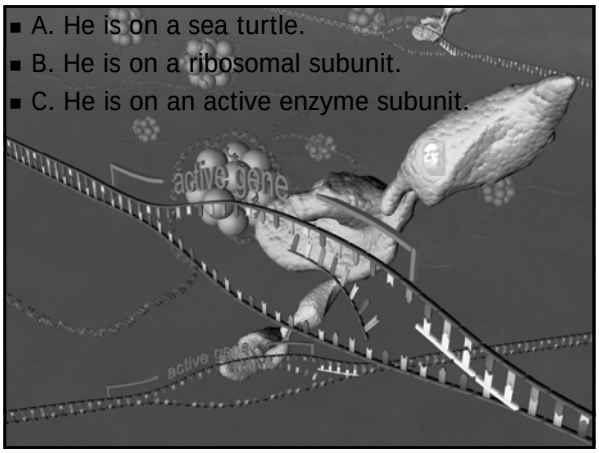




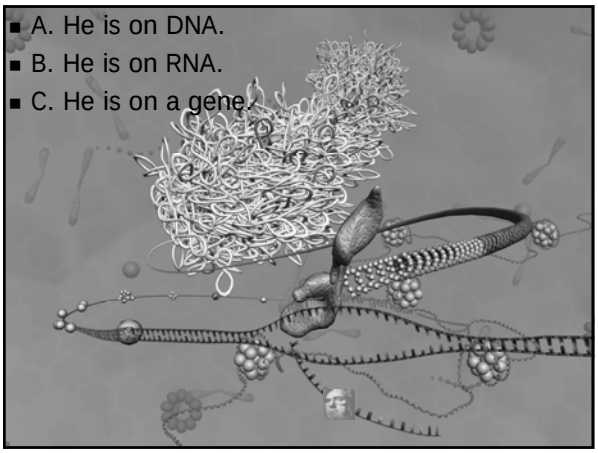




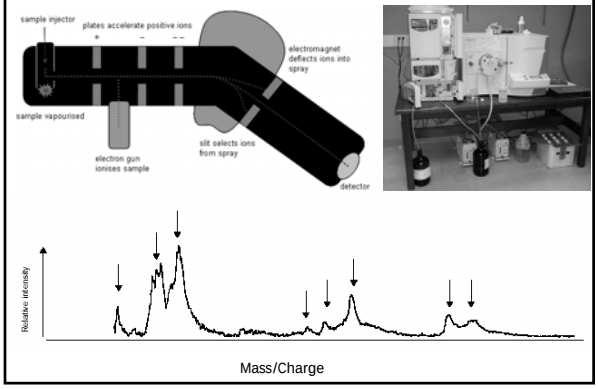
- A. He is on a sea turtle.
- B. He is on a ribosomal subunit.
- C. He is on an active enzyme subunit.



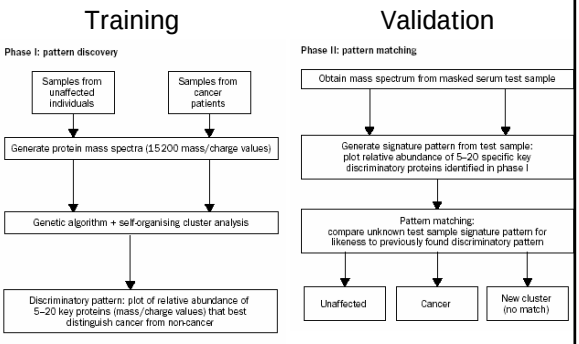
- A. He is on DNA.
- B. He is on RNA.
- C. He is on a gene.



Proteomics: Mass Spectrometer

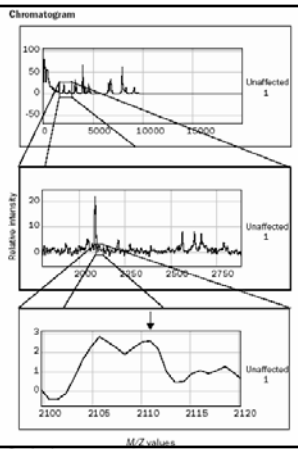


Data Analysis



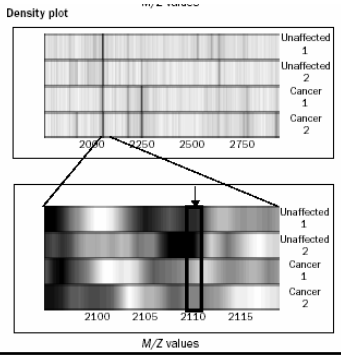
OvaCheck

- Quest Diagnostics and LabCorp:
  - Will analyze blood samples sent by doctors, rather than sell test kits to doctors and hospitals
  - Tests performed at a central location do not require F.D.A. approval
  - Cost: $100-$200



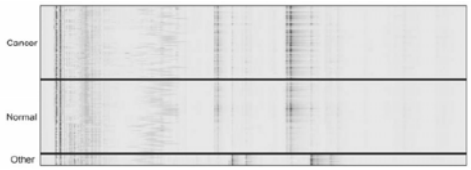
Useful M/Z:
534
989
2111
2251
2465

Comparative Analysis



Useful M/Z:
534
989
2111
2251
2465

Lance Liotta, lead author:
"The most important next goal is validating the promise of these results in large, multi-institutional trials."

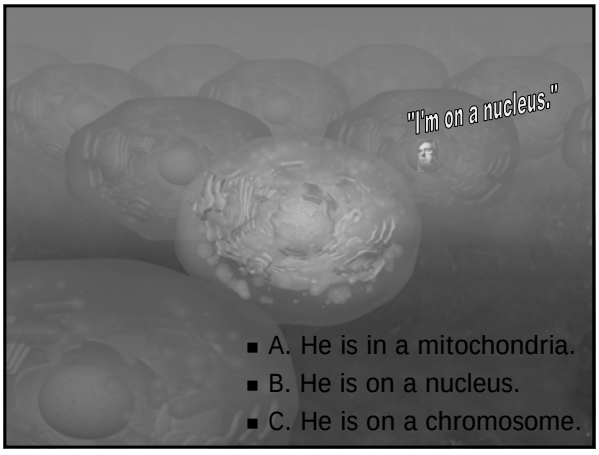


Response

- Dr. Eleftherios P. Diamandis, head of clinical biochem at Mount Sinai Hospital in Toronto.
  - "If you don't know what you're measuring, it's a dangerous black-box technology... They are rushing into something and it could be a disaster."
- Dr. Nicole Urban, head of gynecologic cancer research at the Fred Hutchinson Cancer Research Center in Seattle.
  - "Certainly there's no published work that would make me tell a woman she should get this test."
- Dr. Beth Karlan, director of gynecologic oncology at Cedars-Sinai Medical Center
  - "Before you mass-market to the uninformed, fearful population, it should be peer-reviewed,"
  - When asked whether she would recommend her patients not get tested, she said: "It doesn't matter what I recommend. They are going to do it anyway."

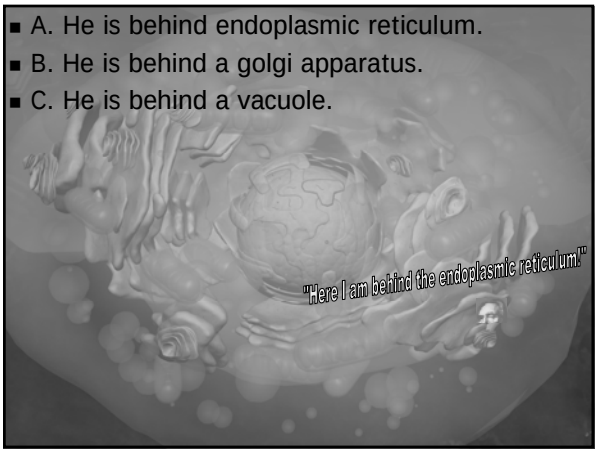
Dr. Koop, where were you?

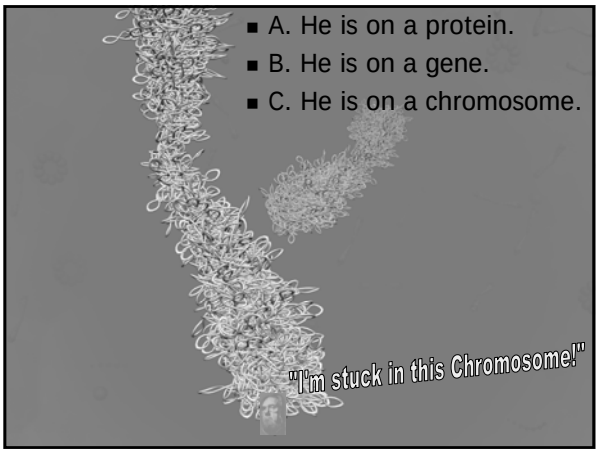
"Let's find out."

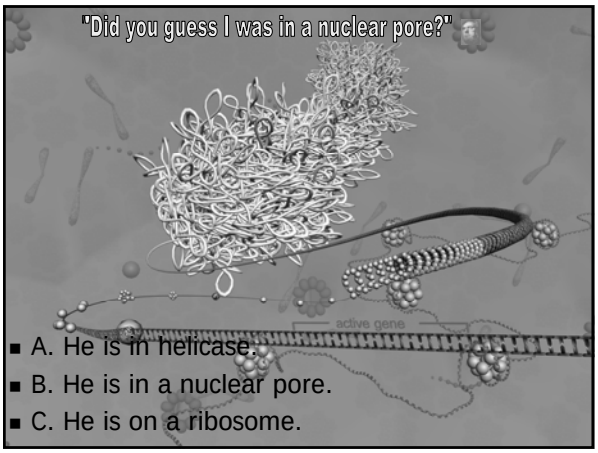


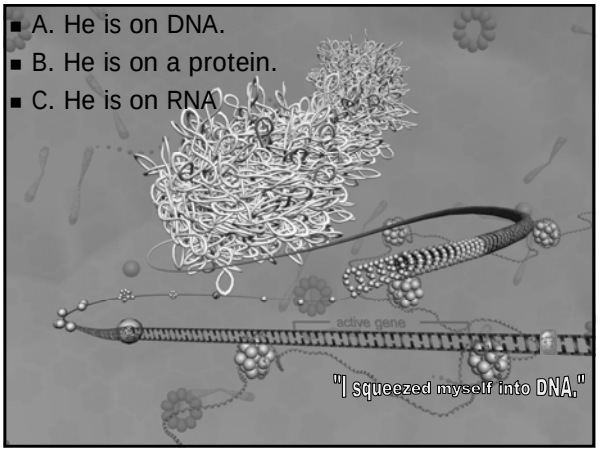
- A. He is in a mitochondria.
- B. He is on a nucleus.
- C. He is on a chromosome.

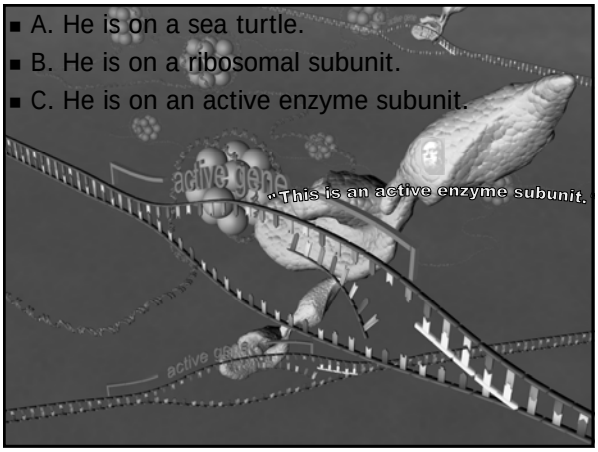
- A. He is behind endoplasmic reticulum.
- B. He is behind a golgi apparatus.
- C. He is behind a vacuole.

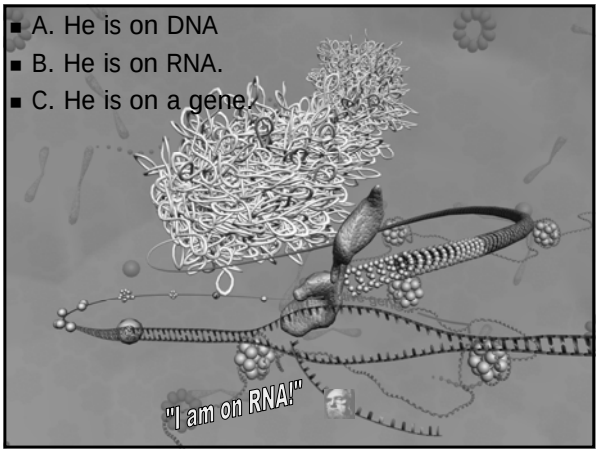




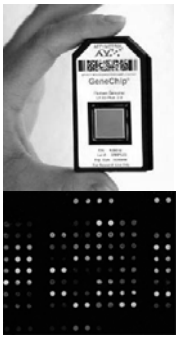


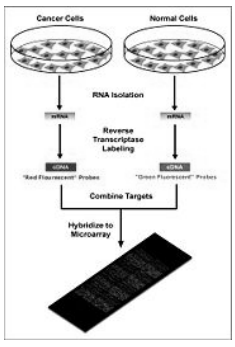






DNA Microarray





New screening technologies

- New screening technologies
  - Proteomics
  - DNA microarrays
  - Optical technologies

BIOE202: Advances in bioengineering

- Advances in Optical Technologies for cancer and point-of-care diagnostics
  - Mark Pierce, March 14 1-2 PM, GRB W211
- Advances in Nanotechnology for cancer and point-of-care diagnostics
  - David Javier, March 21 1-2 PM

Next Time

- HW6 due today
- **Exam 2 is in one week**, March 13th
- Evaluation