OCN Review

CARCINOGENESIS PATHOPHYSIOLOGY DIAGNOSIS AND STAGING

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THINGS TO CONSIDER

- What is the socioeconomic impact of cancer
- Who are the people who have cancer
- What are the risk factors that lead to cancer
- What do we know about cancer cells
- How do we detect cancer
- What might we do to prevent cancer

THE IMPACT OF CANCER

- Cancer is a major public health problem. One in four U.S. deaths due to cancer.
- In **2021**, there will be an **estimated 1.9 million** new **cancer** cases diagnosed in the United States
- **606,570 estimated cancer deaths** for **2021** in the United States.
- In **2019**, approximately **140,690 cancer cases** diagnosed and about **103,250 cancer deaths** among the **oldest old** in the US.
- Cancer in the **oldest old** accounts for **8% of all cases** diagnosed in the US with **17% of all cancer deaths.**

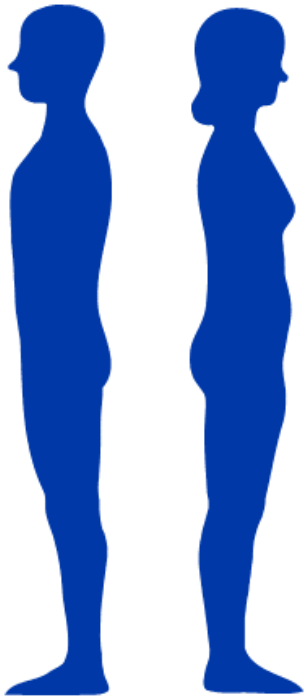
2021 American Cancer Society

THE IMPACT OF CANCER

- Places a high economic burden on society.*
  - National Cancer Institute estimates that cancer-related cost were183 billion in 2015 and are projected to increase to 246 billion in 2030, a 34% increase based upon population growth and aging alone
  - Economic burden on patients
  - Lost productivity
  - Loss of contribution to family and significant others

Estimated New Cancer Cases* in the US in 2021

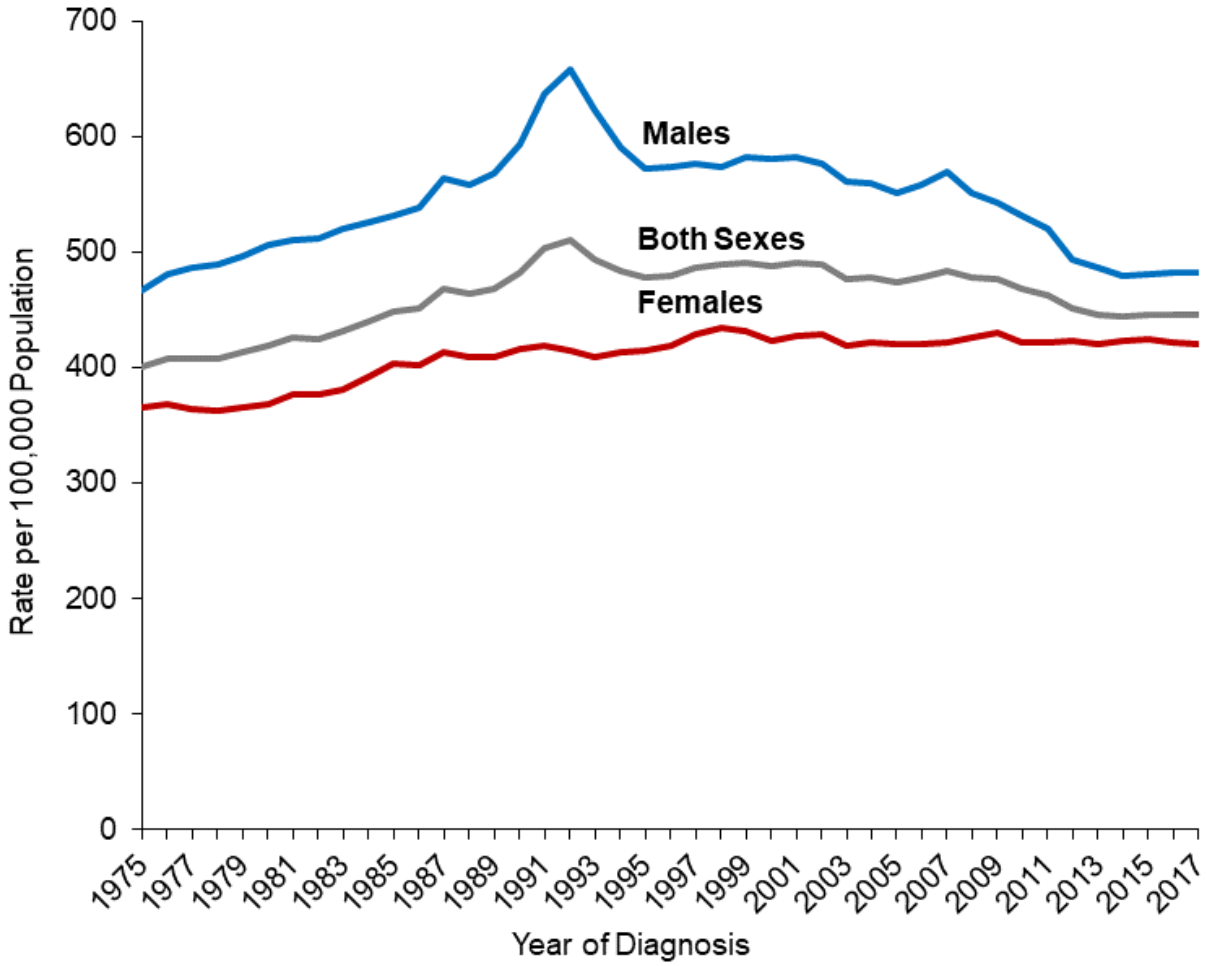
Males 970,250	
Prostate	26%
Lung & bronchus	12%
Colon & rectum	8%
Urinary bladder	7%
Melanoma of the skin	6%
Kidney & renal pelvis	5%
Non-Hodgkin lymphoma	5%
Oral cavity & pharynx	4%
Leukemia	4%
Pancreas	3%
All other sites	20%



Females 927,910	
30%	Breast
13%	Lung & bronchus
8%	Colon & rectum
7%	Uterine corpus
5%	Melanoma of the skin
4%	Non-Hodgkin lymphoma
3%	Thyroid
3%	Pancreas
3%	Kidney & renal pelvis
3%	Leukemia
21%	All other sites

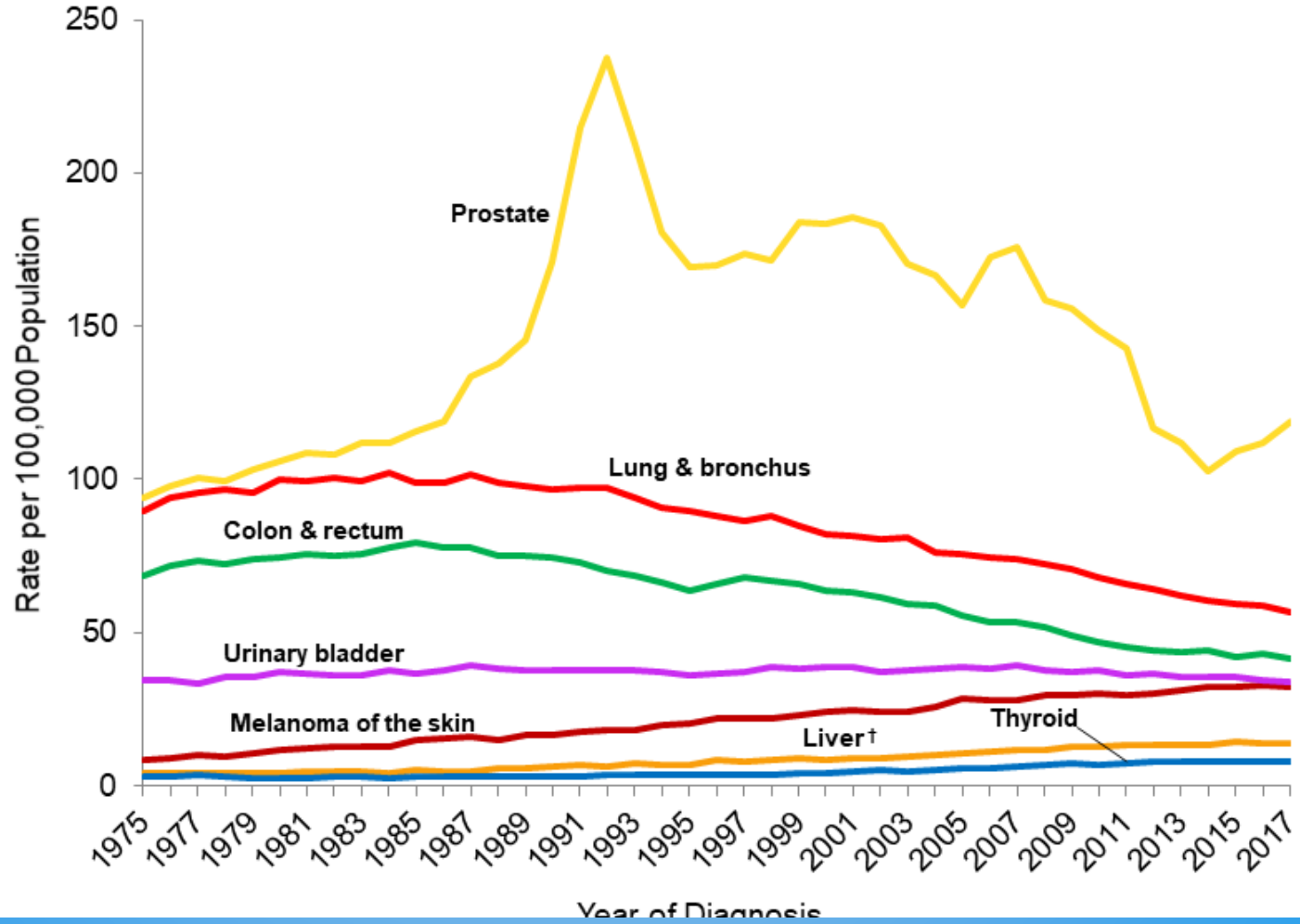
*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

Trends in Cancer Incidence Rates*, US, 1975-2017

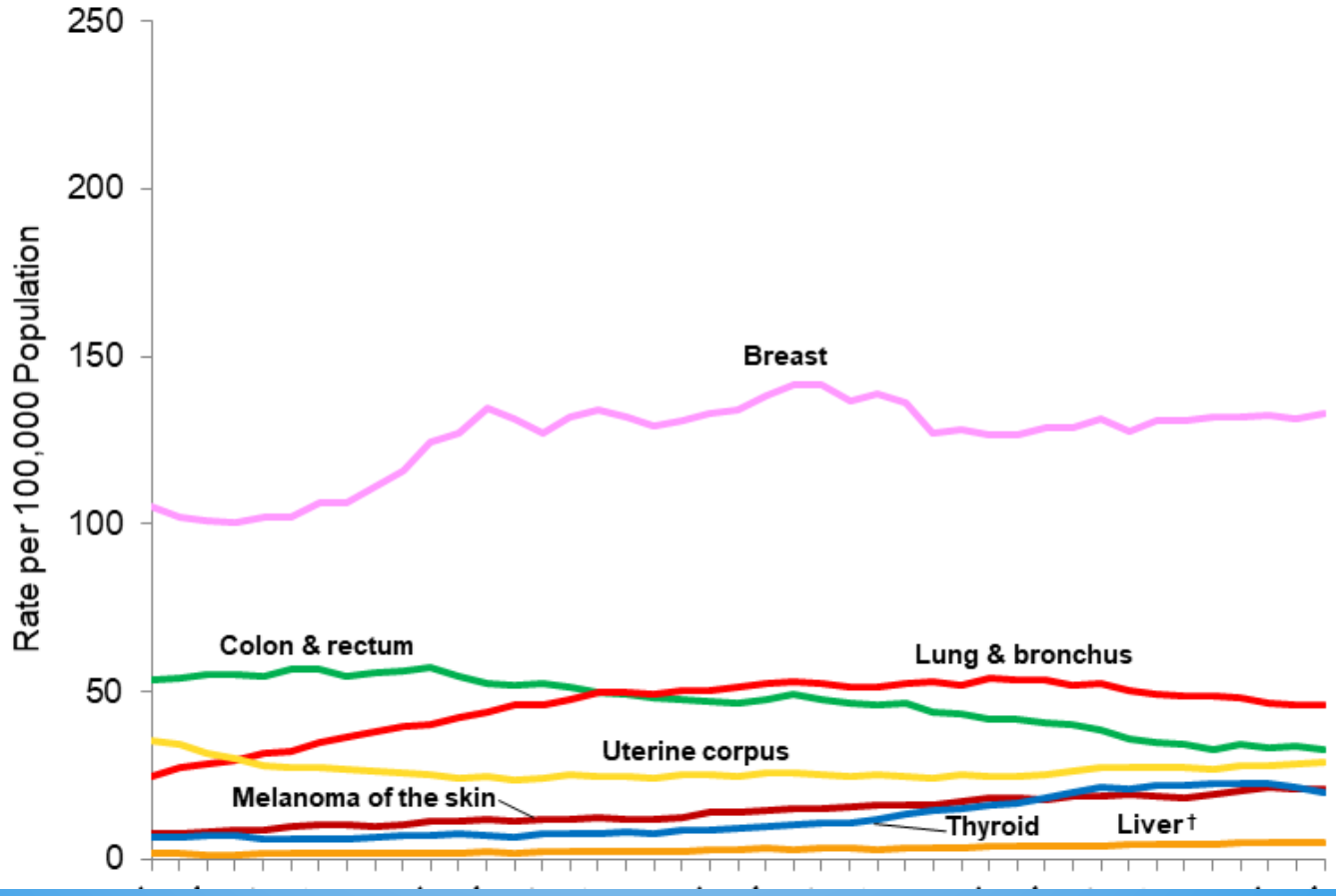


*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute, 2020.

Trends in Cancer Incidence Rates* Among Males, US, 1975-2017



Trends in Cancer Incidence Rates* Among Females, US, 1975-2017

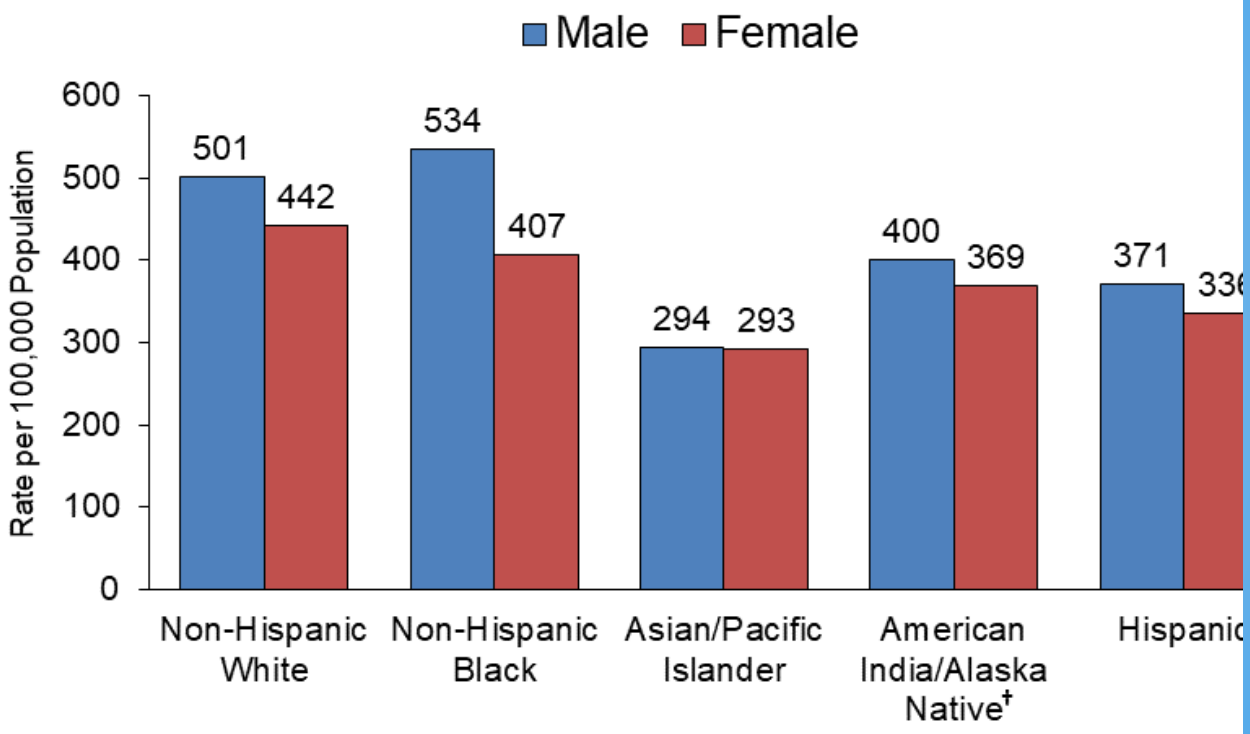


POLL QUESTION:

Which demographic group has the highest cancer incidence rate?

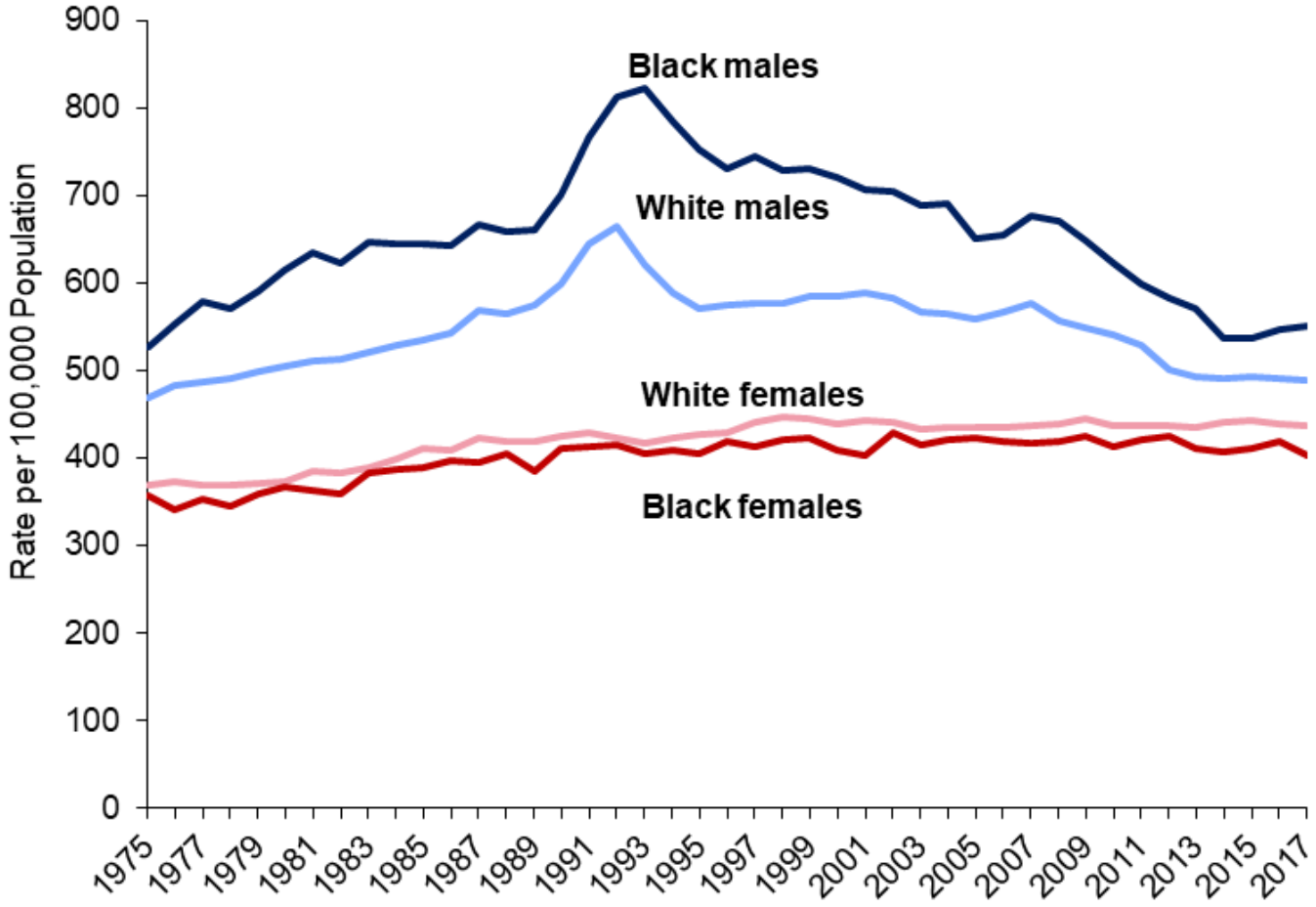
1. White males
2. White females
3. Black males
4. Black females

Cancer Incidence Rates* by Race and Ethnicity, 2013-20



*Age-adjusted to the 2000 US standard population. †Data based on Purchased/Referred Care Delivery Area counties. ‡Persons of Hispanic orig
any race.
Source: North American Association of Central Caner Registries, 2020.

Trends in Cancer Incidence Rates* by Sex and Race, US, 1975-2017



The Lifetime Probability of Developing Cancer for Males, 2015-2017

Site	Risk
All sites*	1 in 2
Prostate	1 in 8
Lung & bronchus	1 in 15
Colon & rectum	1 in 23
Urinary bladder†	1 in 26
Melanoma of the skin‡	1 in 27
Non-Hodgkin lymphoma	1 in 42
Kidney & renal pelvis	1 in 46
Leukemia	1 in 55
Oral cavity & pharynx	1 in 60
Pancreas	1 in 60

*All sites exclude basal cell and squamous cell skin cancers and in situ cancers except urinary bladder. †Includes invasive and in situ cancer cases

The Lifetime Probability of Developing Cancer for Females, 2015-2017

Site	Risk
All sites*	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 17
Colon & rectum	1 in 25
Uterine corpus	1 in 32
Melanoma of the skin†	1 in 40
Non-Hodgkin lymphoma	1 in 52
Thyroid	1 in 53
Pancreas	1 in 62
Leukemia	1 in 78
Ovary	1 in 82

Trends in Five-year Relative Survival Rates (%), 1975-2016

Site	1975-1977	1987-1989	2010-2016
All sites	49	55	67
Breast (female)	75	84	90
Colorectum	50	60	65
Leukemia	34	43	64
Lung & bronchus	12	13	21
Melanoma of the skin	82	88	93
Non-Hodgkin lymphoma	47	51	73
Ovary	36	38	49
Pancreas	3	4	10
Prostate	68	83	98
Urinary bladder	72	79	77

Five-year Relative Survival Rates (%) by Race, 2010-2016

Site	White	Black	Absolute Difference
All Sites	68	62	6
Breast (female)	91	82	9
Colorectum	65	59	6
Esophagus	21	14	7
Non-Hodgkin lymphoma	73	68	5
Oral cavity & pharynx	68	50	18
Ovary	48	41	7
Prostate	98	96	2
Urinary bladder	77	64	13
Uterine cervix	68	56	12
Uterine corpus	84	63	21

POLL QUESTION:

Which cancer has the highest projected death rate for males in 2021?

1. Prostate
2. Brain
3. Colon/rectum
4. Lung & Bronchus

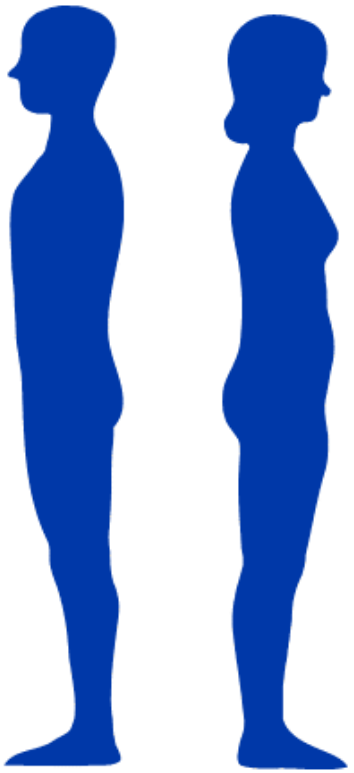
POLL QUESTION:

Which cancer has the highest projected death rate for females in 2021?

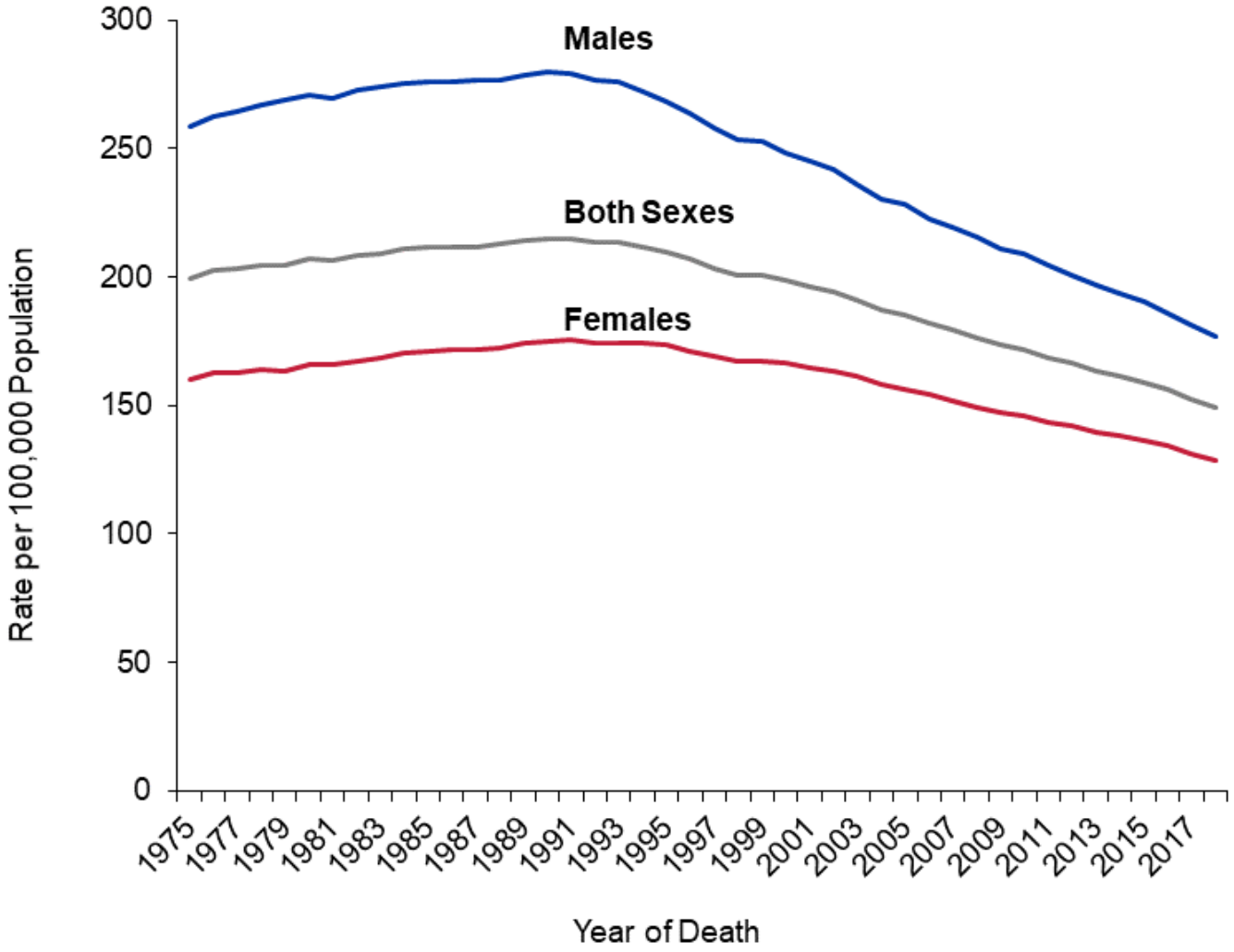
1. Breast
2. Pancreas
3. Colon/rectum
4. Lung & Bronchus

Estimated Cancer Deaths in the US in 2021

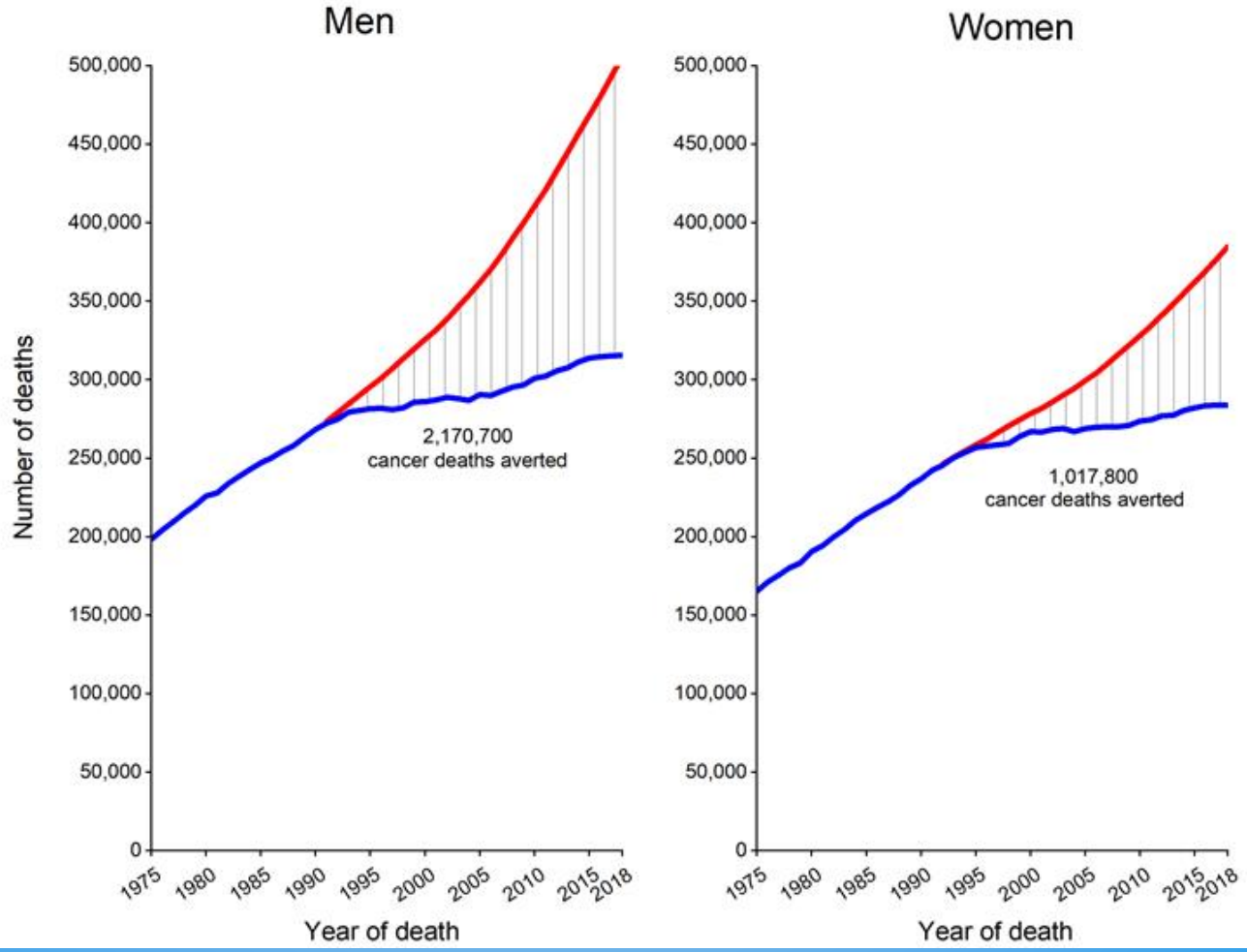
Males 319,420		Females 289,150	
Lung & bronchus	22%	22%	Lung & bronchus
Prostate	11%	15%	Breast
Colon & rectum	9%	8%	Colon & rectum
Pancreas	8%	8%	Pancreas
Liver & intrahepatic bile duct	6%	5%	Ovary
Leukemia	4%	4%	Uterine corpus
Esophagus	4%	3%	Liver & intrahepatic bile duct
Urinary bladder	4%	3%	Leukemia
Non-Hodgkin lymphoma	4%	3%	Non-Hodgkin lymphoma
Brain & other nervous system	3%	3%	Brain & other nervous system
All other sites	25%	26%	All other sites



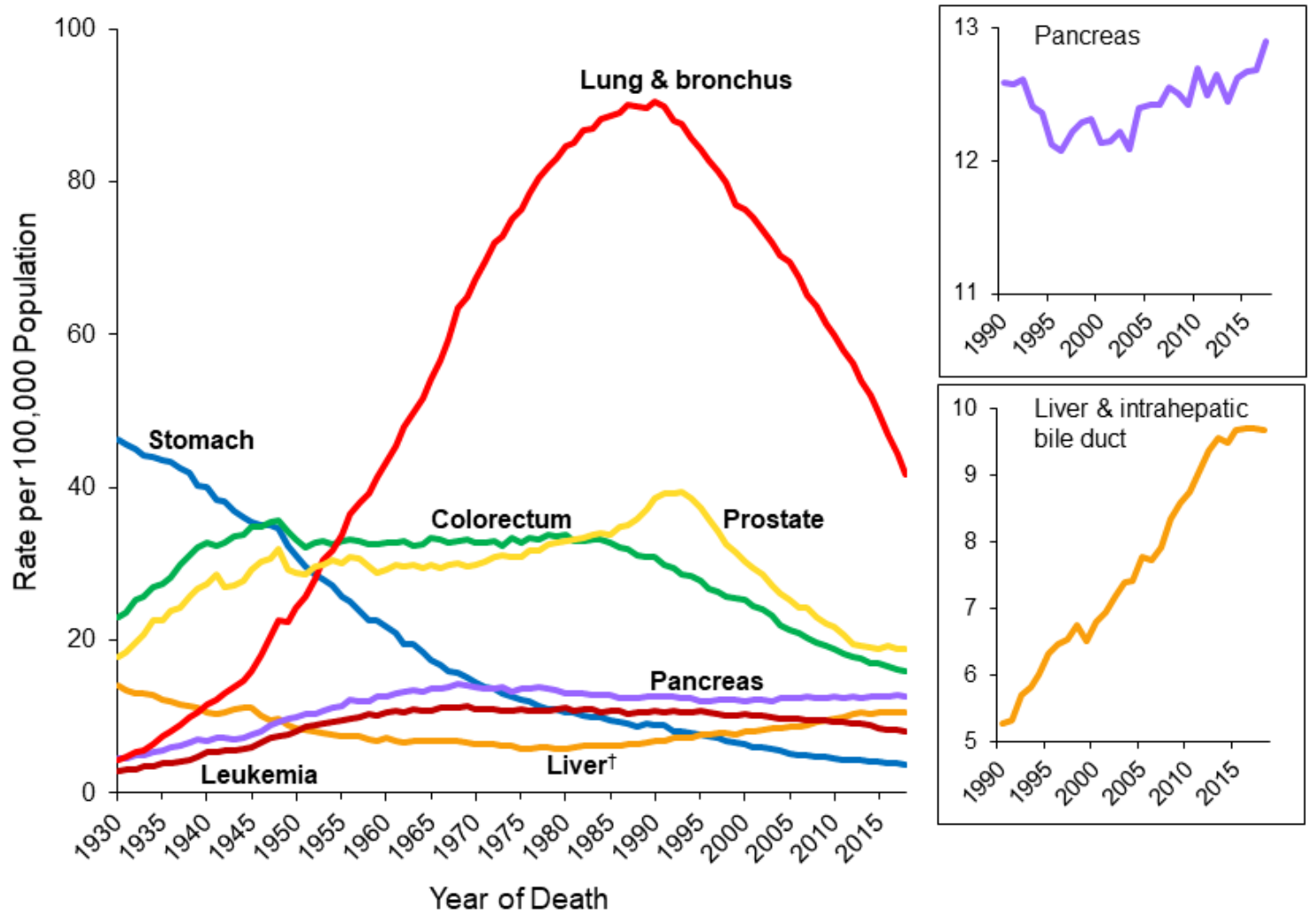
Trends in Cancer Death Rates* by Sex, US, 1975-2018



Total Number of Cancer Deaths Averted from 1991 to 2018

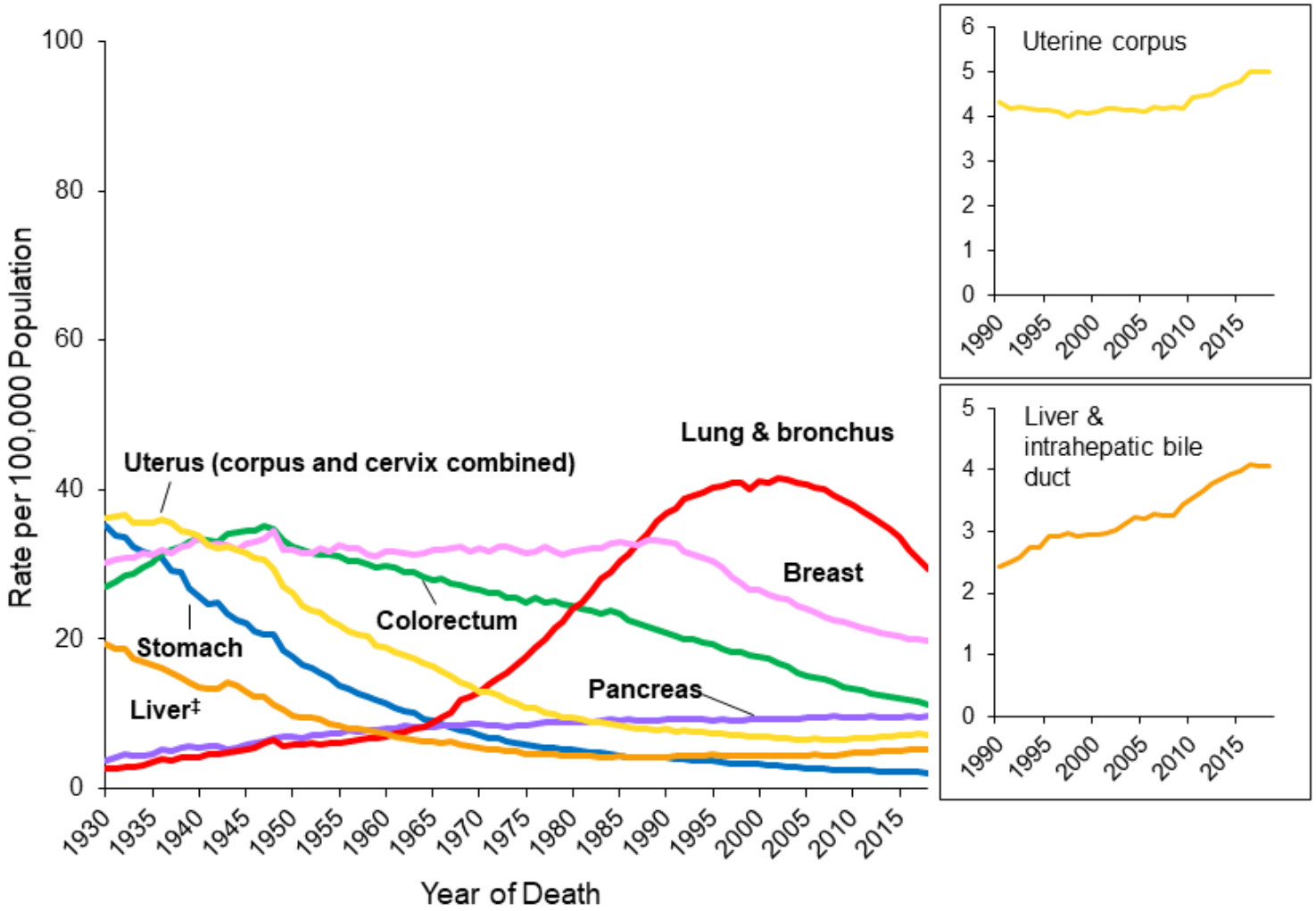


Trends in Cancer Death Rates* Among Males, US,1930-2018

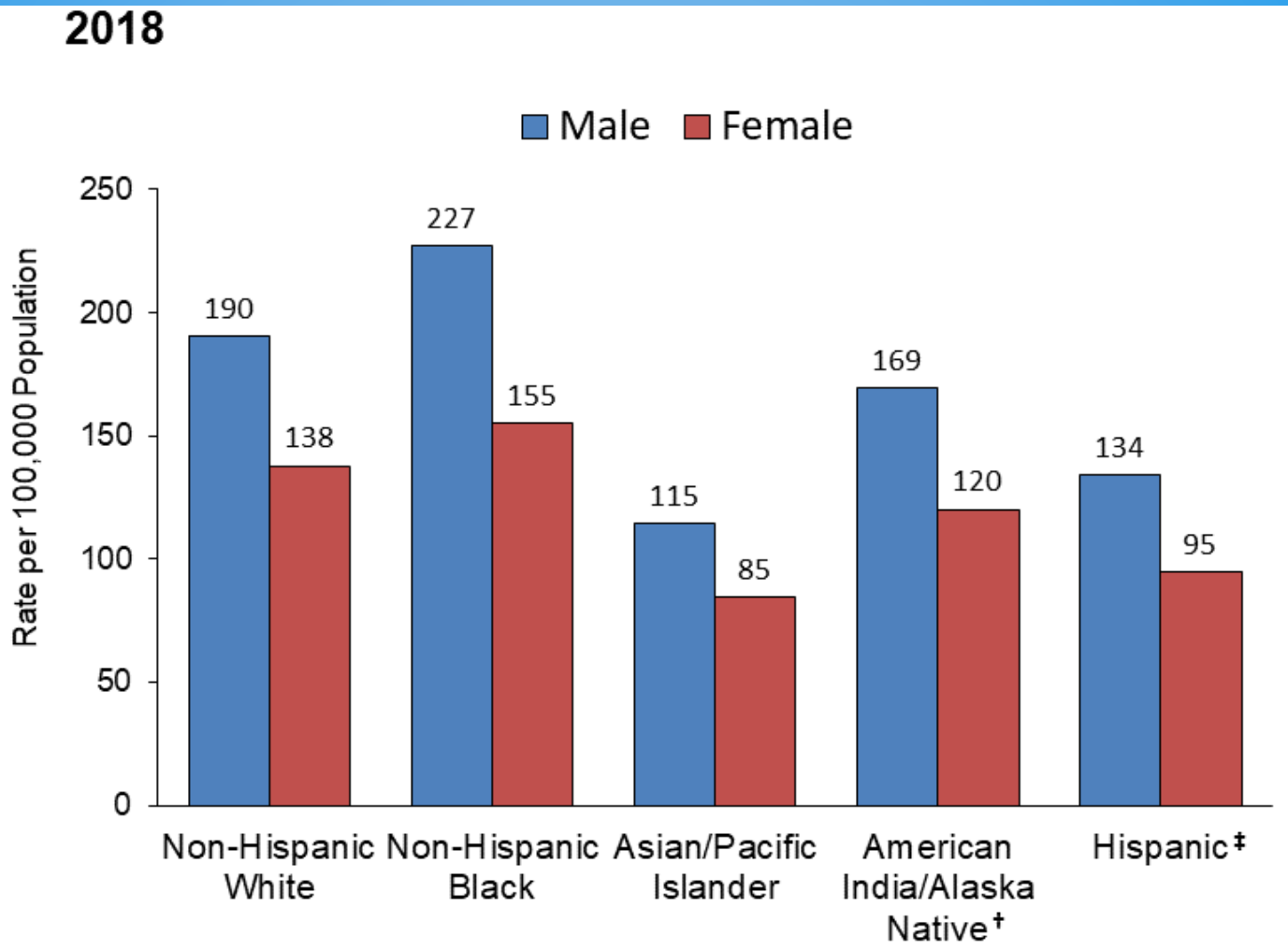


*Age-adjusted to the 2000 US standard population. †Includes intrahepatic bile duct, gallbladder, and other biliary

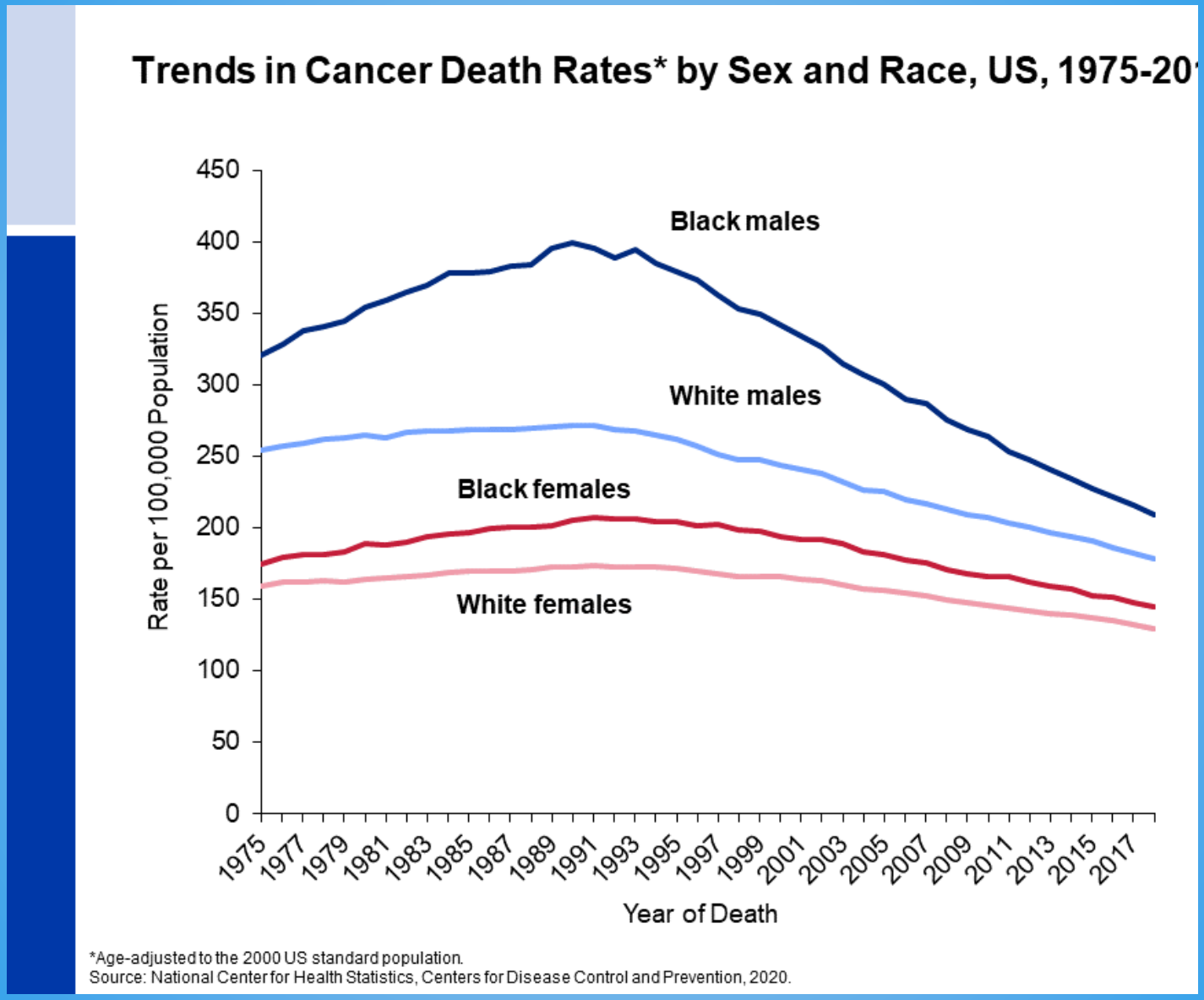
Trends in Cancer Death Rates* Among Females, US,1930-2018



*Age-adjusted to the 2000 US standard population. †Includes intrahepatic bile duct, gallbladder, and other biliary.
NOTE: Due to International Classification of Diseases coding changes, numerator information for colorectal, liver, lung, and uterine cancers has changed over time.



*Per 100,000, age-adjusted to the 2000 US standard population. †Data based on Purchased/Referred Care Delivery Area counties. ‡Persons of Hispanic origin may be of any race.
Sources: National Center for Health Statistics, Centers for Disease Control and Prevention, 2020.


Trends in Cancer Death Rates* by Sex and Race, US, 1975-20
Black males
White males
Black females
White females
Rate per 100,000 Population
450
400
350
300
250
200
150
100
50
0
1975
1977
1979
1981
1983
1985
1987
1989
1991
1993
1995
1997
1999
2001
2003
2005
2007
2009
2011
2013
2015
2017
Year of Death
*Age-adjusted to the 2000 US standard population.
Source: National Center for Health Statistics, Centers for Disease Control and Prevention, 2020.

Common Cancer Types in the United States

Cancer Type	Estimated New Cases	Estimated Deaths
Bladder	81,400 *	17,980 *
Breast (Female-Male)	276,480 – 2620 *	42,170 – 520 *
Colon and Rectal (Combined)	156,540 *	66,700 *
GYN Cancers	113,520 *	33,620 *
Kidney (Renal Cell and Renal Pelvis Cancer)	73,750 *	14,830 *
Leukemia (All Types)	63, 530 *	23,100 *
Liver and Intrahepatic Bile Duct	42,810	30,160 *
Lung (Including Bronchus)	228,820 *	135,720 *
Melanoma	32,270	12,830
Non-Hodgkin Lymphoma	74,240 *	19,940 *
Pancreatic	57,600*	47,050*
Prostate	101,930 *	33,330 *
Thyroid	52,070	2,180

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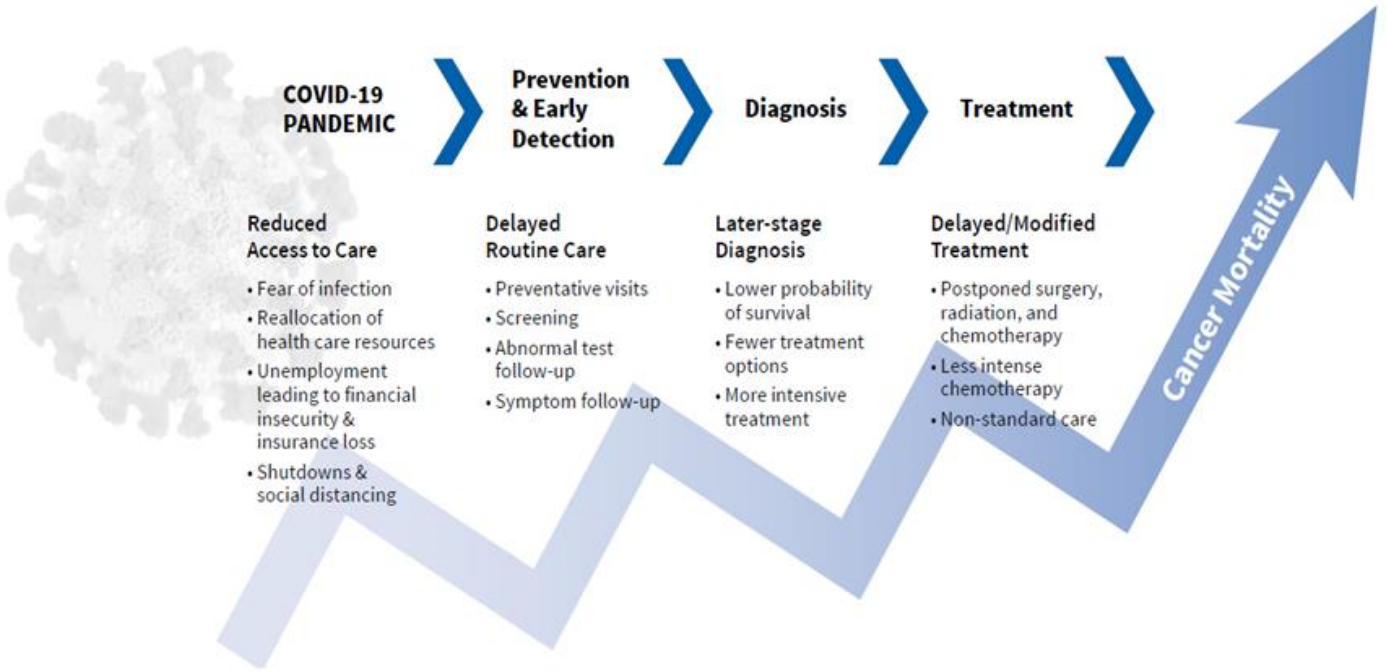
Thyroid	52,070	2,180

American Cancer Society: Cancer Facts and Figures 2019. Atlanta, Ga: American Cancer Society, 2020

Table 2. Estimated Number* of New Cases for Selected Cancers by State, US, 2020

State	All sites	Female breast	Uterine cervix	Colon & rectum	Uterine corpus	Leukemia	Lung & bronchus	Melanoma of the skin	Non-Hodgkin lymphoma	Prostate	Urinary bladder
Alabama	28,570	4,120	240	2,460	780	810	4,230	1,550	1,000	3,530	1,090
Alaska	2,960	510	†	320	120	90	400	120	120	340	160
Arizona	36,730	5,630	260	3,010	1,240	990	4,200	2,380	1,500	3,830	1,810
Arkansas	17,200	2,430	140	1,540	500	630	2,760	800	650	1,860	760
California	172,040	30,650	1,630	15,530	7,030	6,060	18,040	10,980	8,200	20,160	7,780
Colorado	27,290	4,530	190	2,040	920	910	2,550	1,920	1,150	3,140	1,250
Connecticut	20,300	3,590	130	1,520	910	400	2,650	1,110	930	2,320	1,080
Delaware	6,660	960	†	470	220	230	890	420	260	770	320
Dist. of Columbia	3,600	510	†	250	120	110	300	90	130	370	80
Florida	150,500	19,900	1,130	11,310	4,460	3,370	18,150	8,750	7,170	13,950	6,780
Georgia	55,190	8,340	440	4,660	1,710	1,550	7,240	3,190	2,280	6,840	2,110
Hawaii	6,800	1,300	60	730	330	230	870	520	290	700	300
Idaho	8,540	1,340	60	730	310	340	990	740	390	1,160	470
Illinois	71,990	11,020	540	6,240	2,850	2,400	9,210	3,700	2,920	8,000	3,310
Indiana	37,940	5,410	270	3,410	1,430	1,290	5,700	2,370	1,590	3,570	1,720
Iowa	18,460	2,710	110	1,600	700	840	2,440	1,150	800	1,920	870
Kansas	16,170	2,390	110	1,320	560	620	2,020	890	650	1,730	640
Kentucky	26,500	3,800	200	2,440	870	920	4,890	1,330	1,040	2,440	1,130
Louisiana	26,480	3,910	260	2,370	690	930	3,700	1,030	1,110	2,970	1,050
Maine	8,180	1,370	50	670	390	160	1,430	520	390	800	520
Maryland	34,710	5,500	250	2,570	1,300	820	3,930	1,780	1,330	4,410	1,360
Massachusetts	36,990	6,690	220	2,650	1,630	580	5,150	2,190	1,670	3,890	1,970
Michigan	61,770	8,800	360	4,620	2,380	2,060	8,140	3,290	2,450	6,820	2,890
Minnesota	33,210	4,670	140	2,320	1,200	1,600	3,580	1,750	1,350	2,880	1,460
Mississippi	17,190	2,390	160	1,730	450	500	2,510	620	570	2,050	630
Missouri	37,540	5,360	270	3,090	1,290	1,370	5,540	1,820	1,410	3,540	1,580
Montana	5,850	960	†	500	220	250	770	450	250	680	330
Nebraska	10,560	1,580	70	940	390	480	1,270	610	450	980	470
Nevada	16,540	2,310	130	1,480	480	520	1,850	840	650	1,780	780
New Hampshire	8,060	1,350	†	590	370	180	1,220	530	370	910	510

Potential Impact of the COVID-19 Pandemic on Future Cancer Outcomes



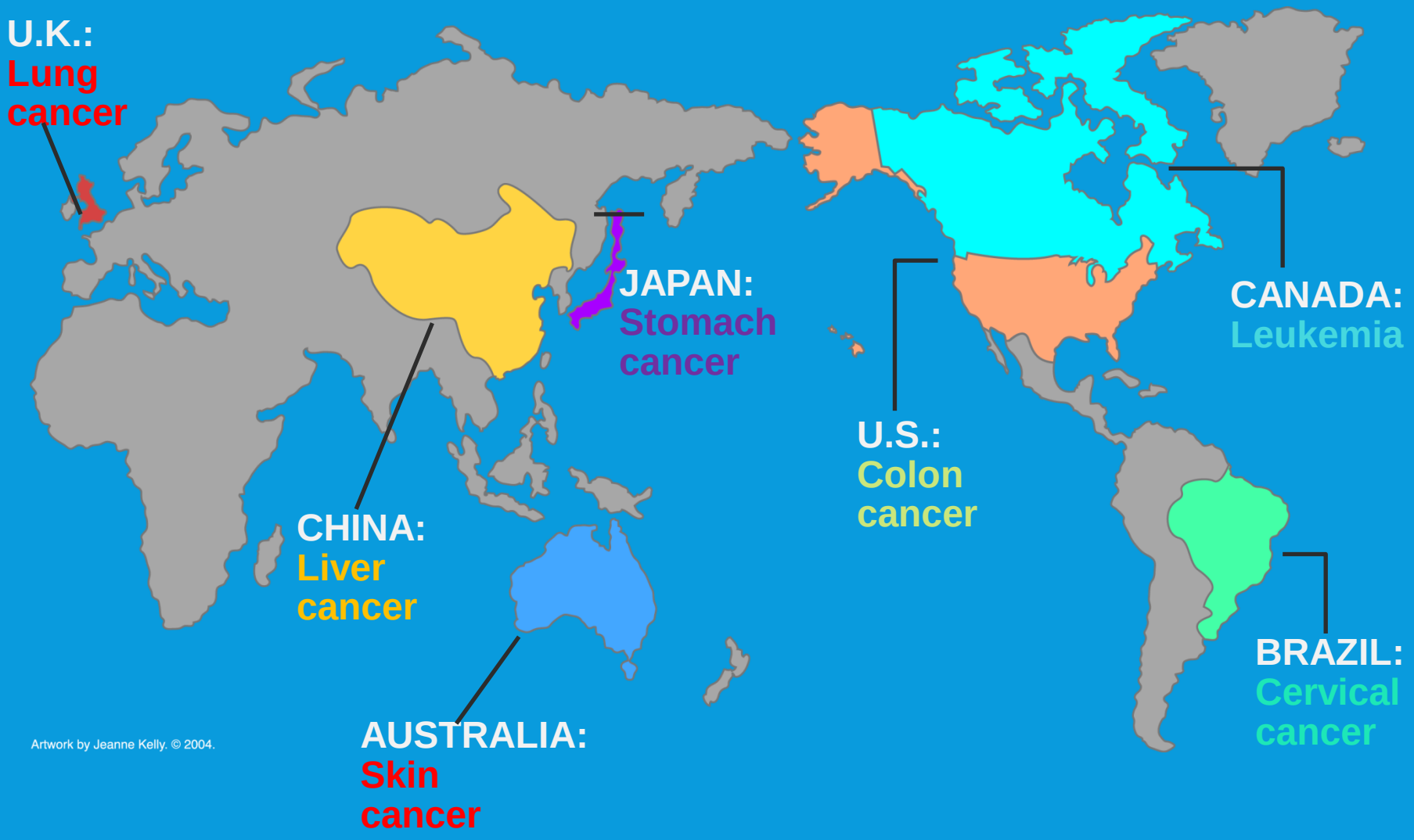
Coronavirus image courtesy of CDC.

CANCER THROUGHOUT THE WORLD

- 2000: 10 million new cases and 6 million deaths due to cancer
- 2020: 15 million new cases and 12 million deaths due to cancer
- Estimate 70% of cancer-related deaths will occur in developing countries due to poor resources
- 80-90% of cancer patients in developing countries will have incurable cancer at time of diagnosis, leading to long-term survival rates about half of those in the U.S.

Population-Based Studies

Regions of Highest Incidence



EPIDEMIOLOGY

- **World Health Organization (WHO)**
- **American Cancer Society (ACS)**
- **National Cancer Institute SEER Program**
- **www.SEER.cancer.gov**
- **S**urveillance, **E**pidemiology and **E**nd **R**esults
  - Incidence
  - Prevalence
  - Mortality rate
    - patient demographics
    - primary tumor site
    - tumor morphology
    - stage at diagnosis

FAST STATS

- Fast Stats is an interactive tool for quick access to key SEER and US cancer statistics for major cancer sites by age, sex, race/ethnicity and data type. Statistics are presented as graphs and tables

TERMINOLOGY

- **Incidence**
  - The number of new cases of a specific type occurring in a specific population in one year
- **Mortality**
  - The number of deaths of a specific type occurring in a specific population in one year
- **Prevalence**
  - The number of people alive on a certain date who previously had a diagnosis of cancer .
- **Survival**
  - In general, defined as people with NED at 5 years

THE GOOD NEWS . . .

- The death rate from all cancers combined has decreased by 1.5% per year for men since 1993, and by 0.8% per year for women since 1992.
- The mortality rate has continued to decrease from the three most common sites in men (lung, colorectal, and prostate), and from breast and colorectal cancers in women.

MORE GOOD NEWS . .

- Advances in molecular and cellular biology are broadening our understanding of carcinogenesis, and new treatment modalities are being developed accordingly.

- There are nearly 10 million cancer survivors today.

MORE GOOD NEWS . .

- **More targeted therapies:**
  - As more is learned about the molecular biology of cancer, researchers will have more targets for their new drugs.
  - Along with more monoclonal antibodies and small signaling pathway inhibitors
    - new classes of molecules –
      - antisense oligodeoxynucleotides
      - small interfering RNA (siRNA).

MORE GOOD NEWS . .

- **Immunotherapy:**
  - Drugs aimed at specific immune checkpoints are being developed to help the immune system better kill cancer cells.

MORE GOOD NEWS . .

- **More on cancer genetics:**
  - Researchers are looking for gene mutations that cause some patients to respond better to certain drugs.

MORE GOOD NEWS . .

- **Nanotechnology:**
  - New technology for producing materials that form extremely tiny particles is leading to very promising imaging tests that can more accurately show the location of tumors.
  - It also is aiding the development of new ways to deliver drugs more specifically and effectively to cancer cells.

MORE GOOD NEWS . .

- **Robotic surgery:**
  - This term refers to manipulation of surgical instruments remotely by robot arms and other devices controlled by a surgeon.
  - Robotic systems have been used for several types of cancer surgery;
    - radical prostatectomy is among the most common uses in surgical oncology.
  - As mechanical and computer technology improve, some researchers expect future systems will be able to remove tumors more completely and with less surgical trauma.

MORE GOOD NEWS . .

- **Expression profiling and proteomics:**
  - Expression profiling lets scientists determine relative output of hundreds or even thousands of molecules (including the proteins made by RNA, DNA, or even a cell or tissue) at one time.
  - Knowing what proteins are present in cells can tell scientists a lot about how the cell is behaving.
  - In cancer, it can help distinguish more aggressive cancers from less aggressive ones and can often help predict which drugs the tumor is likely to respond to.

MORE GOOD NEWS . .

- **Expression profiling and proteomics:**
  - Proteomic methods are also being tested for cancer screening.
  - For most types of cancer, measuring the amount of one protein in the blood is not very good at finding early cancers.
  - Researchers are hopeful that comparing the relative amounts of many proteins may be more useful, and that finding large amounts of certain proteins and less of others can provide accurate, useful information about cancer treatment and its outcomes.
  - Proteins (and other types of molecules) are even found in exhaled breath, which is now being tested to find out if it can show early signs of lung cancer.
  - This is an exciting area of research and early results in lung and colorectal cancer studies have been promising.

POLL QUESTION:

African Americans are more likely to be diagnosed with cancer at advanced stages of their disease.

1. TRUE
2. FALSE

RACIAL DISPARITIES

- African Americans are more likely to be diagnosed at advanced stages of their disease.
- African American men and women have a greater chance of dying from their disease.
- 5-year relative survival is lower among African Americans than in Whites at every stage of diagnosis and nearly for every cancer site.

RISK FACTORS

- An identifiable trait or habit that is statistically associated with an increased susceptibility for disease

RISK FACTORS

- Viral
  - Hepatitis
  - HPV
  - HIV
  - EBV
  - HTLV-1
- Genetics
  - Heredity
  - Oncogenes
  - Suppressor Genes

RISK FACTORS

- Absolute Risk
  - Expressed as number of cases per 100,000
  - Average
- Relative Risk
  - Relates to one group
- Can you change the numbers???

RISK FACTORS

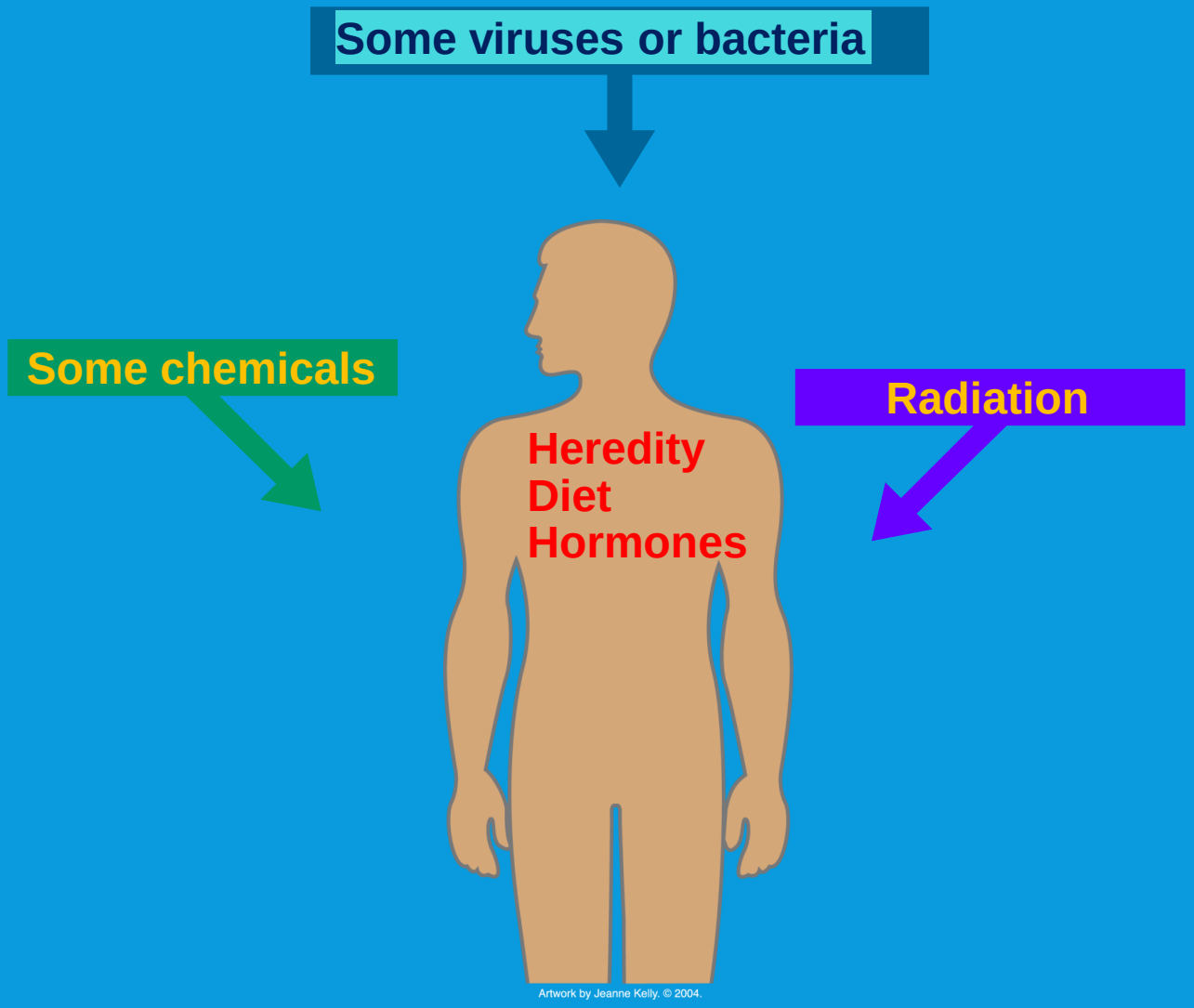
- Modifiable
- Not modifiable
- Cancer is caused by complex interactions between genes and a variety of external factors
- Recognizing risk factors identifies individuals at greater risk for cancer and provides opportunity to intervene or modify risk

POLL QUESTION:

What are the causes of cancer?

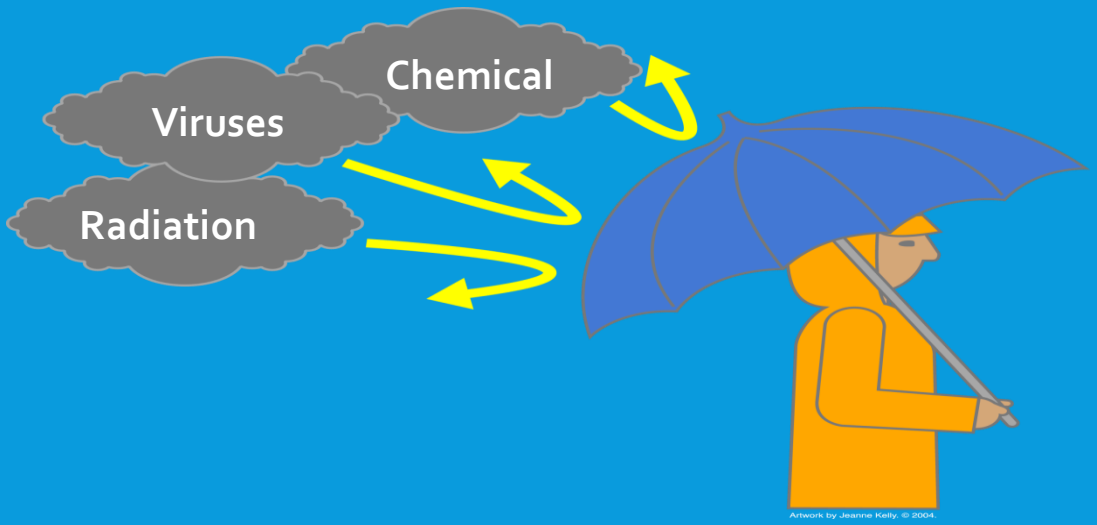
1. Viruses or bacteria
2. Chemicals
3. Radiation
4. Heredity, Diet, Hormones
5. Bad Luck
6. All of the above

What Causes Cancer?



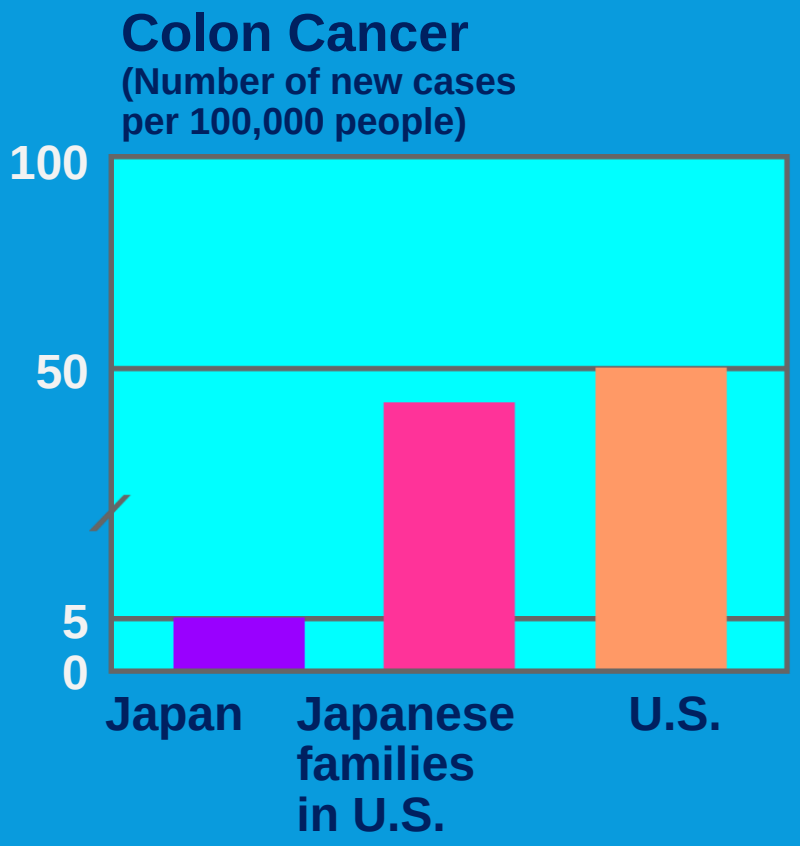
LIFESTYLE RISK FACTORS

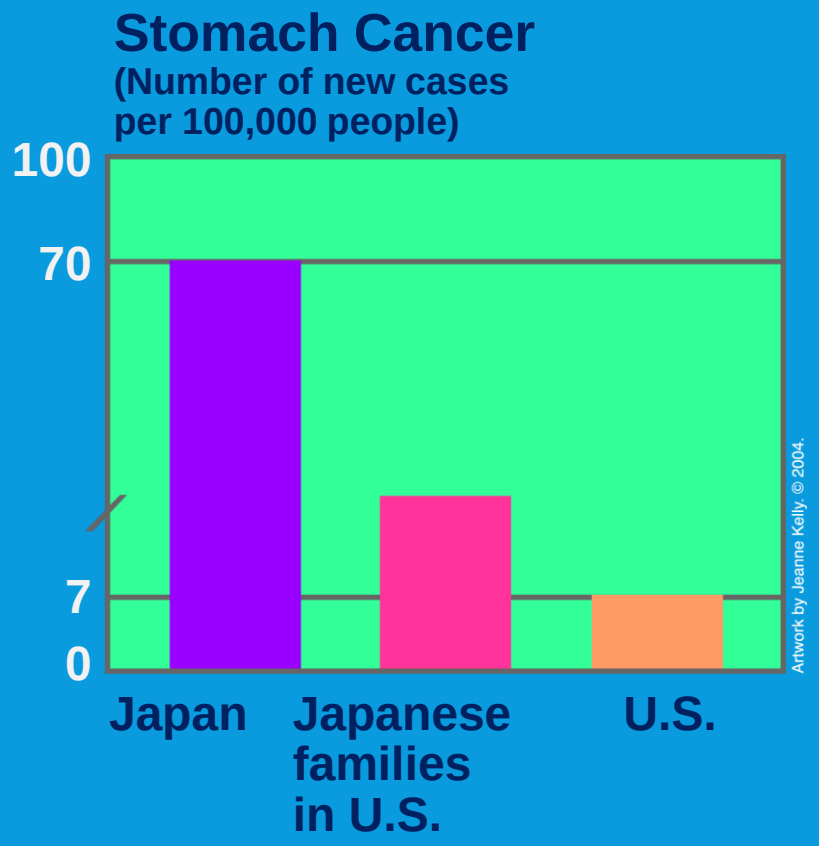
- Diet
- Exercise
- Substance use
- Radiation exposure
- Chemical exposure



- Inherited from one or both parents
- Mutations occur in the germ cells
- These cancers represent very small number of cancers
- Examples
  - Li Fraumeni Syndrome, familial melanoma , retinoblastoma and some colon cancers

Heredity? Behaviors? Other Factors?





MODIFIABLE RISK FACTORS

- Tobacco
- "Second hand "tobacco exposure
  - Workplace,
  - Home
  - Community
- Diet
  - Acrylamide (potato chips, French fries)
  - Red and processed meats/high fat
  - Artificial Sweeteners

MODIFIABLE RISK FACTORS

Environmental pollutants

Radiation

Ionizing

Non-ionizing

MODIFIABLE RISK FACTORS

- Hormones
- Alcohol
- Sedentary lifestyle

GENES

Individual units of hereditary information located at specific positions on a chromosome

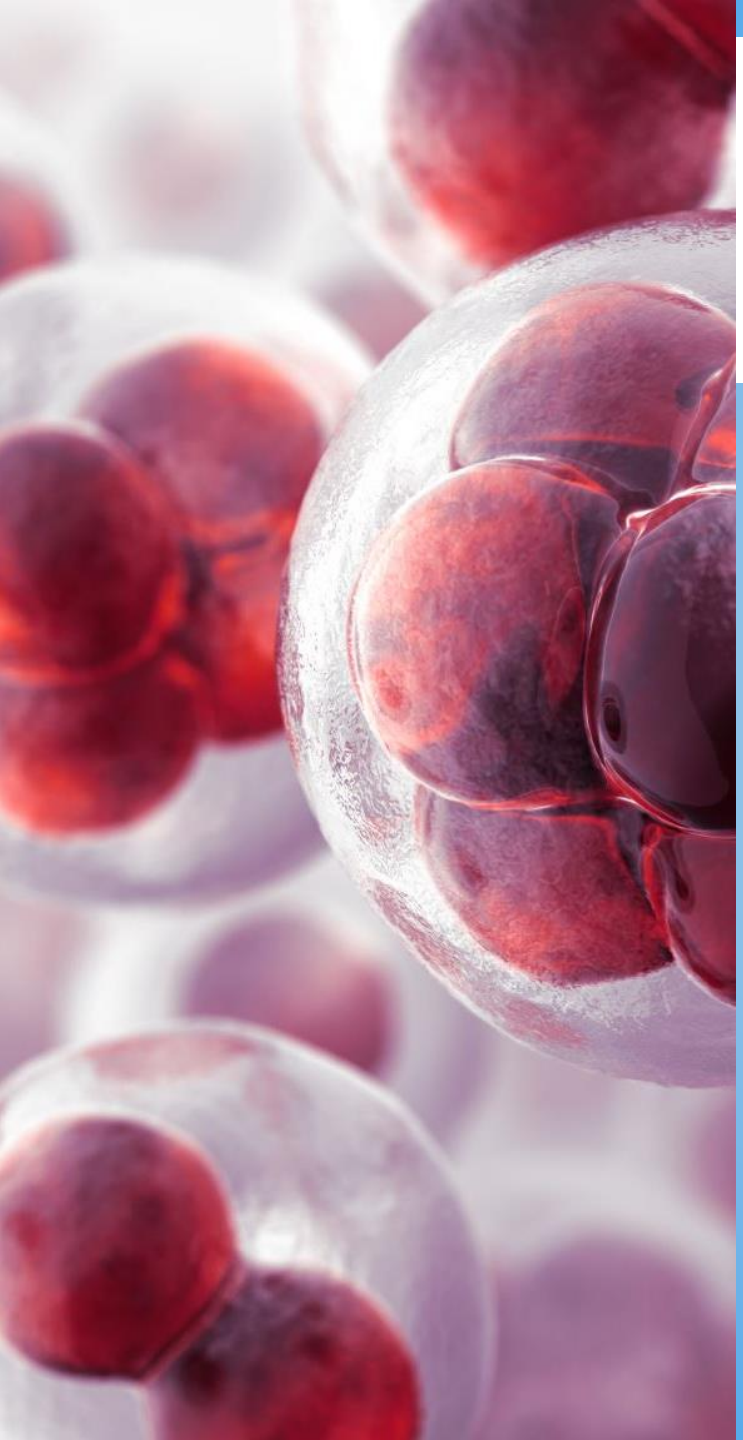
Consist of a sequence of DNA that codes for a specific protein

They code for proteins whose normal function is to correct errors that arise when cells duplicate their DNA prior to cell division.

CYTOGENETICS

Focuses on the structure function and abnormalities of the chromosomes to diagnose both solid and hematologic cancers

Supports a personal approach to diagnose and treat cancers



GENETIC RISK FACTORS

- **Oncogenes may give rise to cancers when they are altered**
  - Suppressor genes :
    - BRCA1 repair
    - BRCA2 repair
  - **Proto-oncogenes**
    - RAS
    - ERB
    - ABL

CHARACTERISTICS OF CELLS

- Regular size and shape
- Function
- Predictable life span
- Genetic programming
- Responsive to bio feedback mechanisms
- Apoptosis (cell death)

NORMAL CELL FUNCTION 101

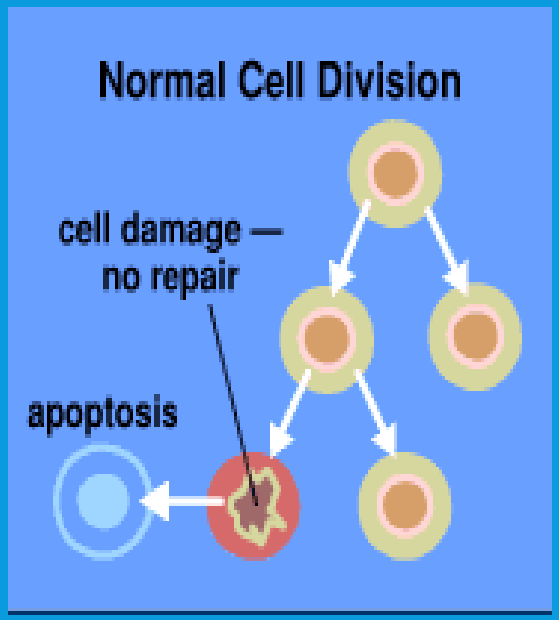
all cells come from preexisting cells

vital functions of an organism occur within cell

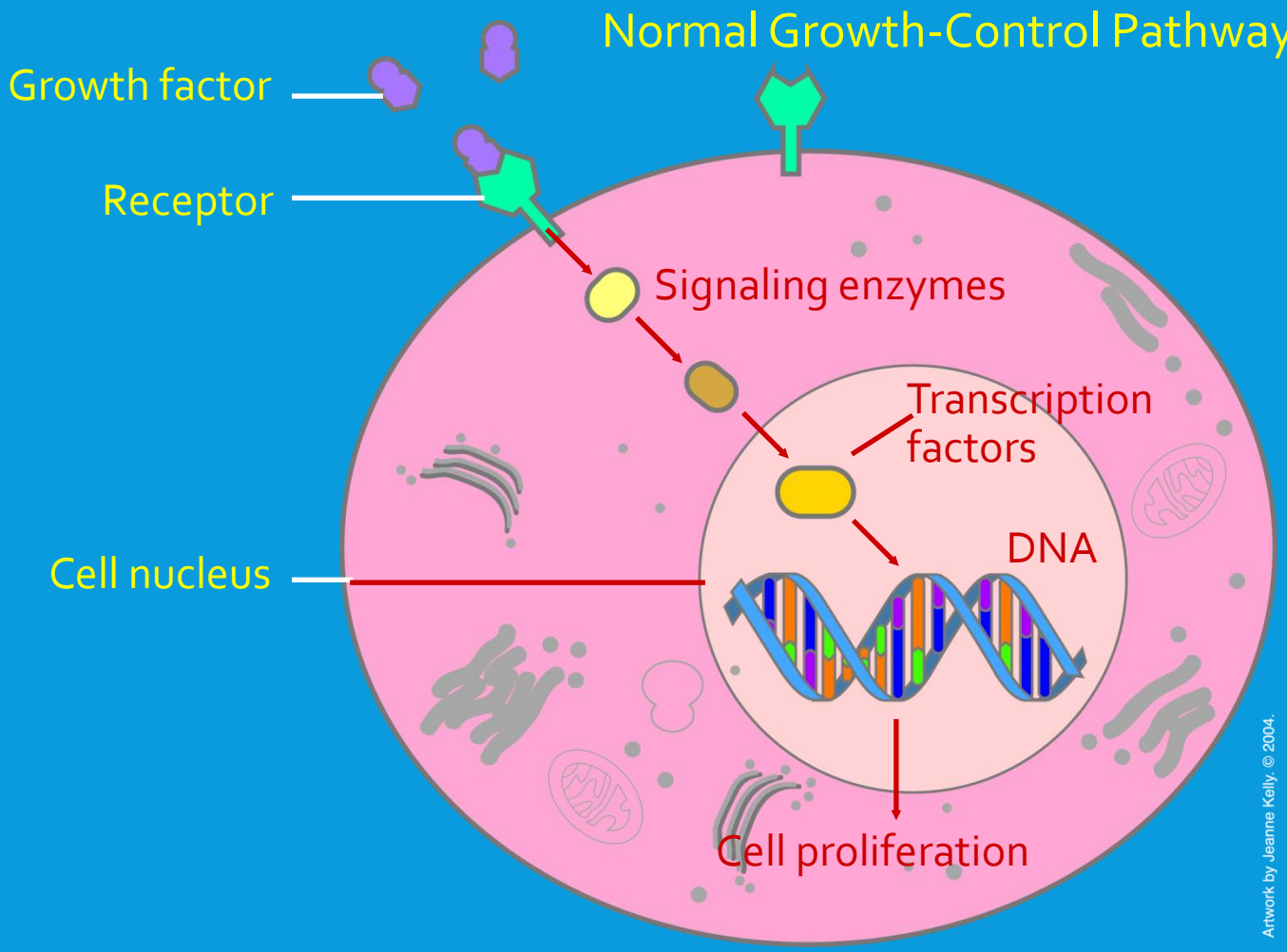
all cells contain the hereditary information necessary for regulating cell functions and for transmitting information to the next generation of cells.

CELL REPLICATION

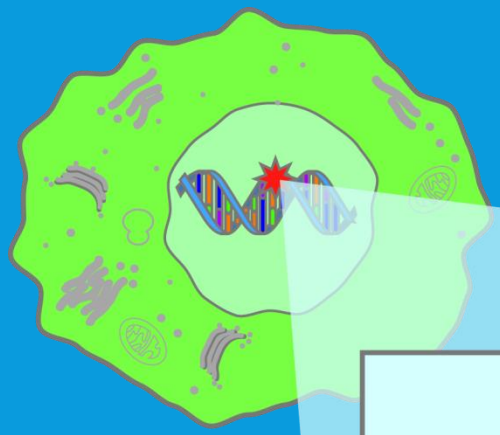
- Occurs billions of times every 24 hours to replace damaged or worn-out cells or produce proteins that support life
- Process "turned on" by growth factors
- Driven and moderated by genes
- Repair genes
  - Surveillance genes
  - Killer (suppressor) genes

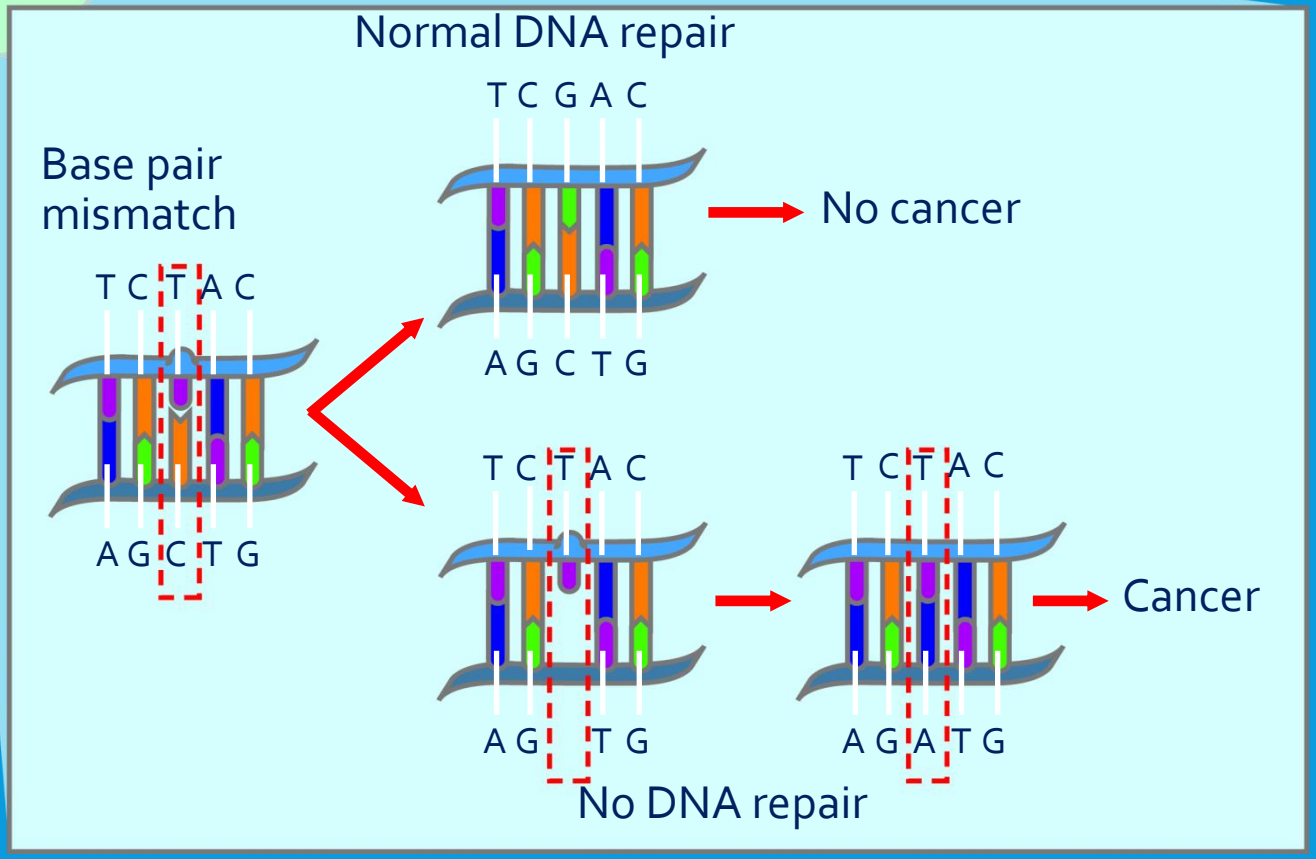


NORMAL CELL REPLICATION



DNA Repair Genes





CANCER CELLS

- DNA damage/Cellular Abnormalities
- Uncontrolled replication
- Dedifferentiation
- Ability to spread
  - Invasion
  - Angiogenesis
  - Metastasis

PROPERTIES OF CANCER CELLS

- **Cytological changes**
  - Size and number
  - Nuclear/cytoplasmic ratio
- **Altered cell growth**
  - Immortality
  - Growth inhibition/cell cycle control
  - Angiogenesis
- **Cell membrane changes**
  - New antigens
  - Over expression of antigen

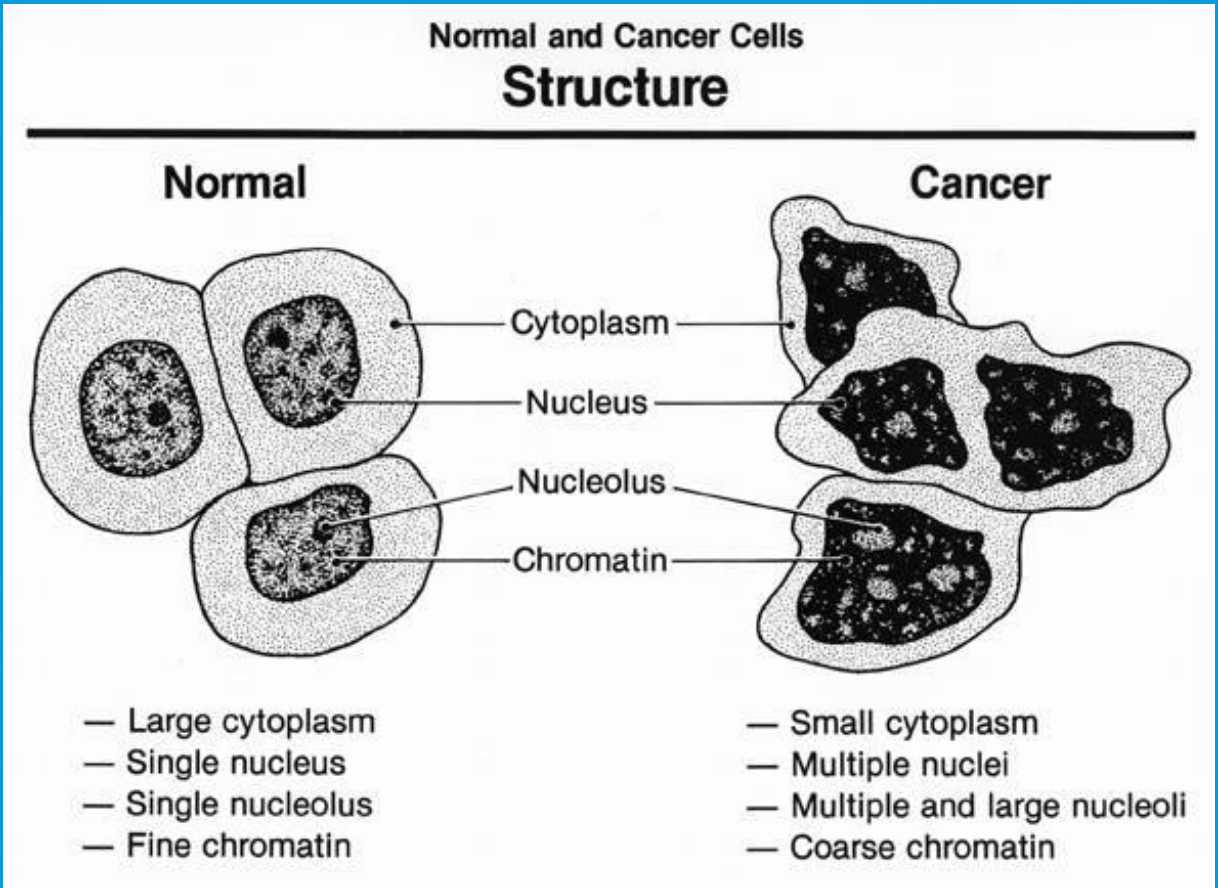
HOW CANCER CELLS DIFFER FROM NORMAL CELLS

- DNA errors
- Reproductive errors
- Dedifferentiation
- Uncontrolled proliferation

EVOLUTION OF A MALIGNANT PROCESS

- **Genetic mutations or injuries**
- **Hormonal influences**
- **Environmental factors**
  - Chemical exposure
  - Radiation
- **Viruses**
- **Bad luck**
- **Cancer is caused by complex interactions between genes and a variety of external factors**

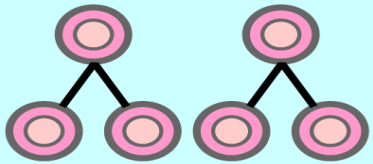
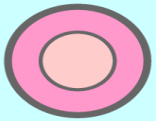
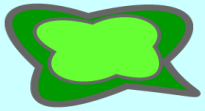
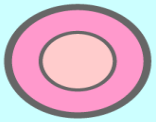
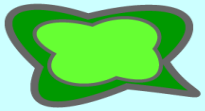
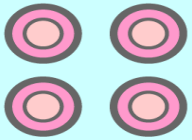
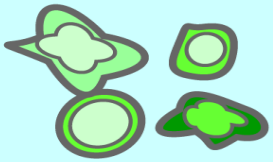
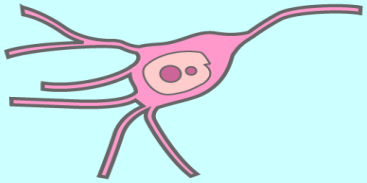
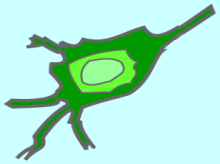
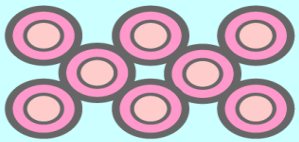
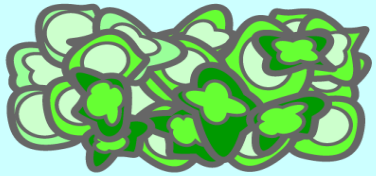
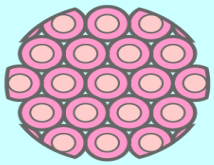
NORMAL VERSUS MALIGNANT



Mutations and Cancer

Genes Implicated in Cancer

The prime suspects	*But*
Mutations in:	Other mutations also occur in:
■ Oncogenes ■ Tumor suppressor genes	■ Cell death genes ■ Cell signaling genes
■ DNA repair genes	■ Cell cycle checkpoint genes
	■ Cellular senescence genes
	■ Cellular differentiation genes
	■ Metastasis/invasion genes
	■ Carcinogen –activating genes –deactivating genes

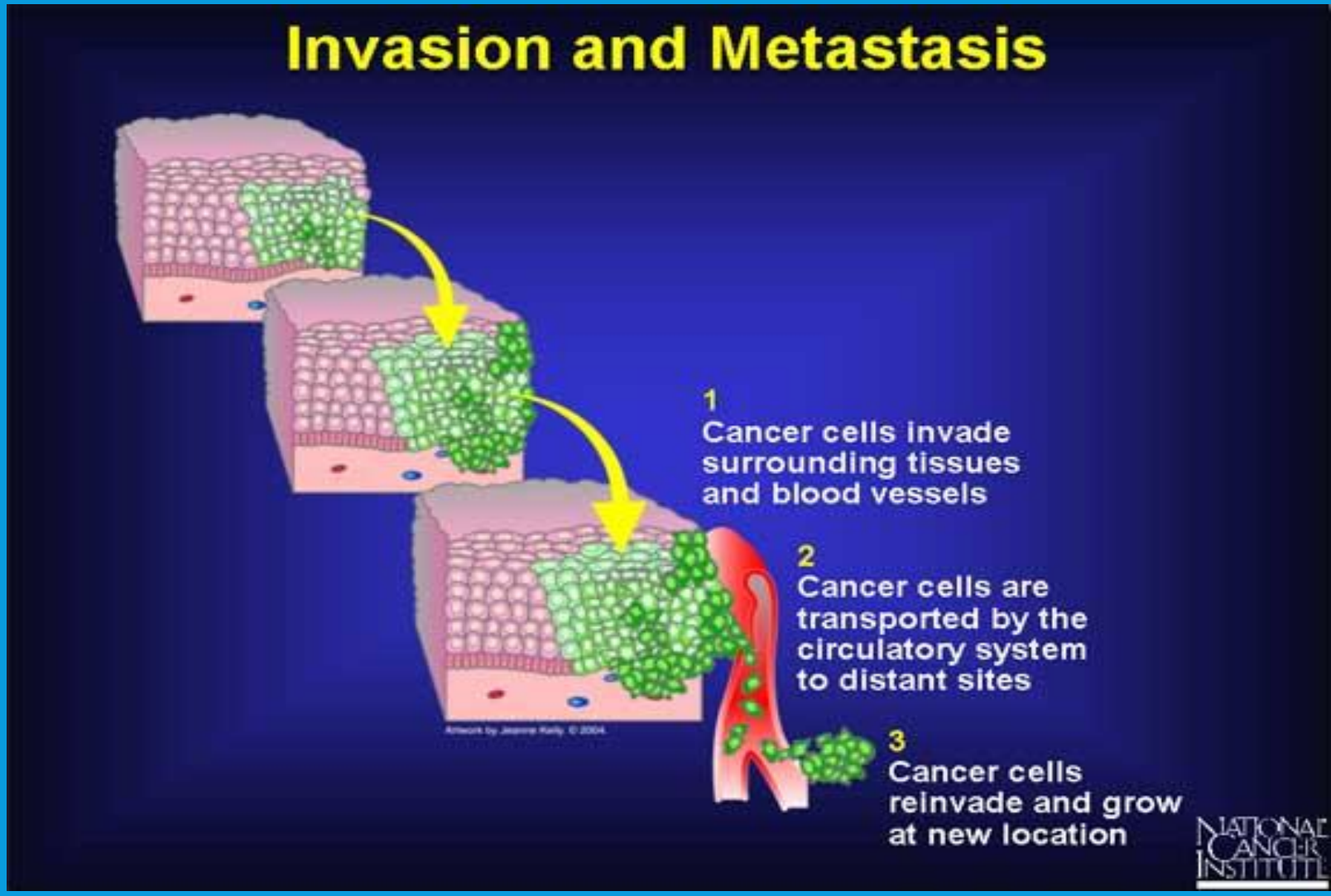
Normal	Cancer	
		Large number of irregularly shaped dividing cells
		Large, variably shaped nuclei
		Small cytoplasmic volume relative to nuclei
		Variation in cell size and shape
		Loss of normal specialized cell features
		Disorganized arrangement of cells
		Poorly defined tumor boundary

Stages of Malignant Transformation

- **Initiation:** irreversible DNA damage.
- **Promotion:** cells with genetic defects start multiplication.

(*Promoters are substances that enhance tumor growth by stimulating proliferation, immune suppression, etc.*).

- **Progression:** neoplastic cells → malignant tumor → invasion of healthy tissue.


Invasion and Metastasis
1
Cancer cells invade surrounding tissues and blood vessels
2
Cancer cells are transported by the circulatory system to distant sites
3
Cancer cells reinvade and grow at new location
NATIONAL CANCER INSTITUTE

MALIGNANT TRANSFORMATION/METASTASIS

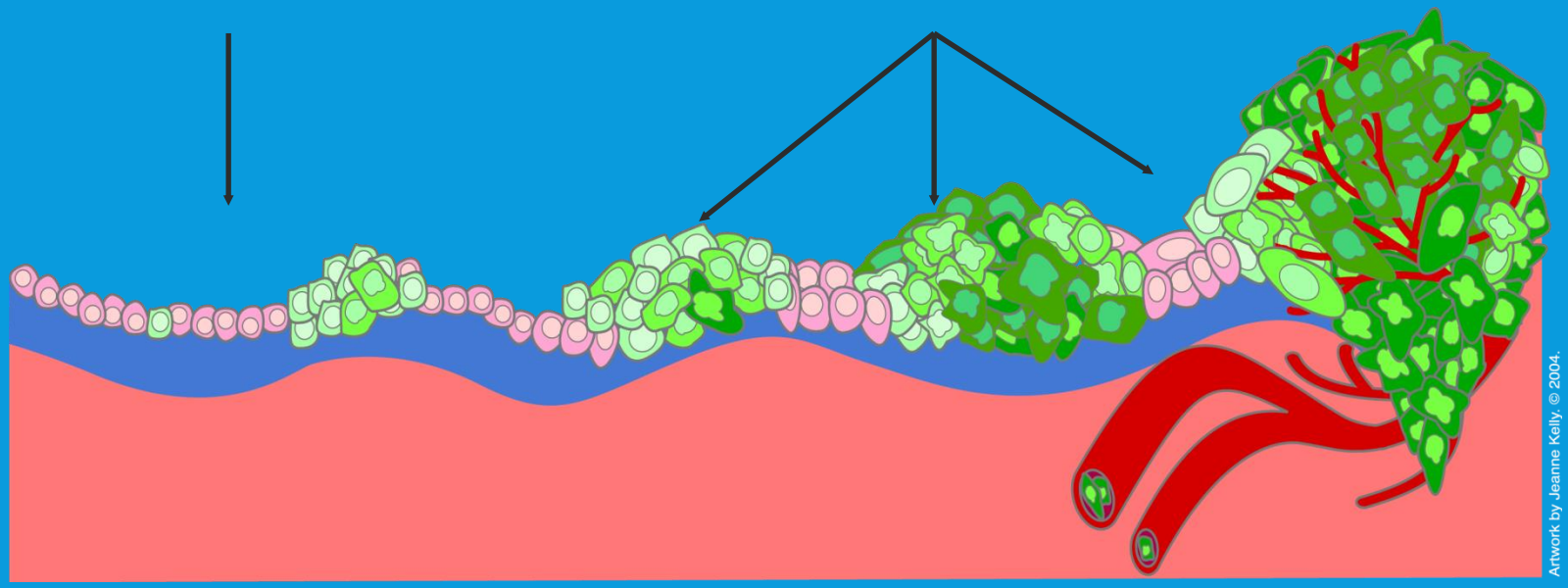
- Detachment
- Invasion
- Survival in transport
- Arrest in distant organ
- Establishment of secondary tumor

- Initiation
  - cell type specific
  - Chemical/radiation/etc.
- Promotion
  - Proliferation free for all
  - Dysplasia, CIS
- Progression

Cancer Tends to Involve Multiple Mutations

Benign tumor cells grow only locally and cannot spread by invasion or metastasis

Malignant cells invade neighboring tissues, enter blood vessels, and metastasize to different sites



Time

Mutation inactivates suppressor gene

Cells proliferate

Mutations inactivate DNA repair genes

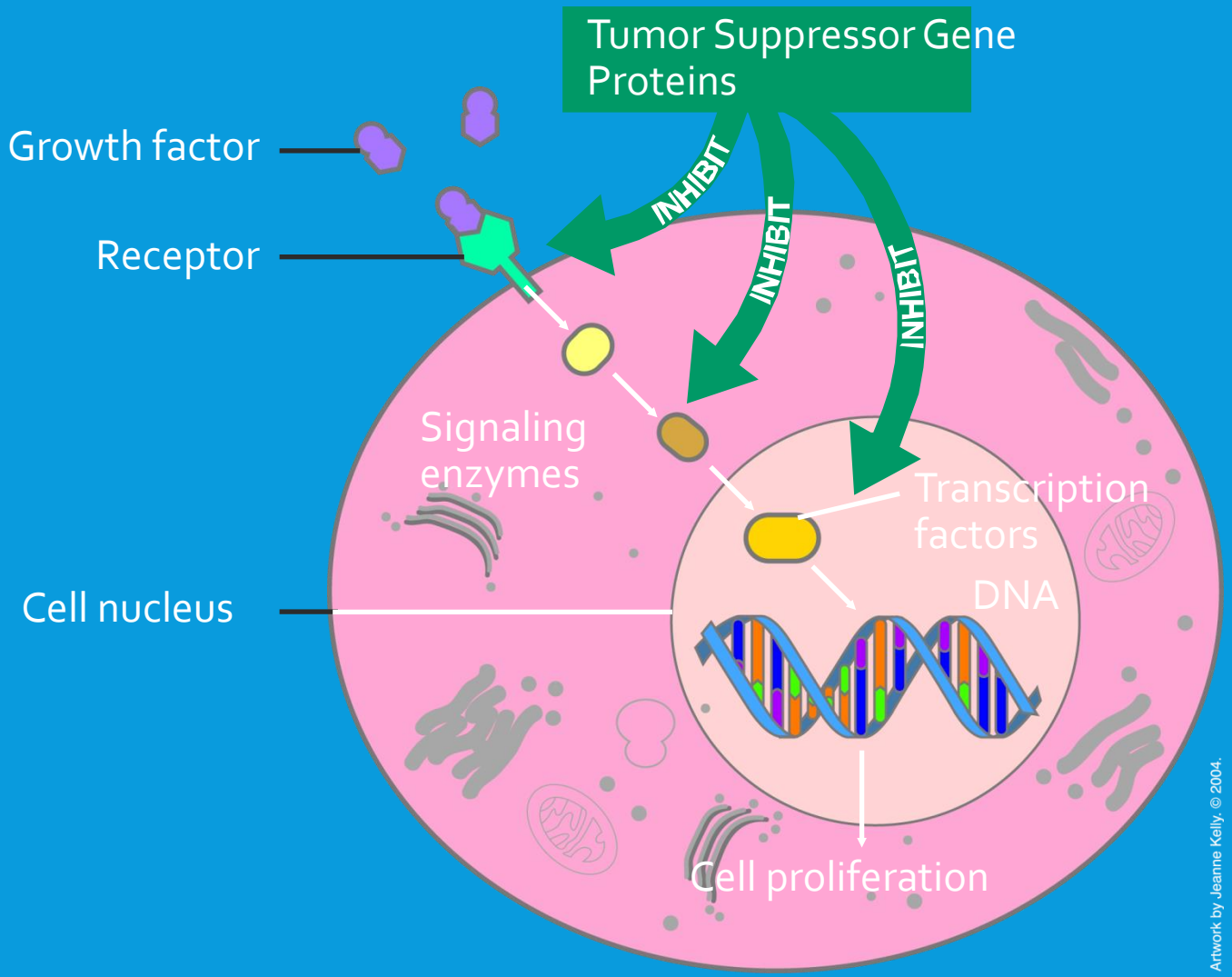
Proto-oncogenes mutate to oncogenes

More mutations & more genetic instability, metastatic disease

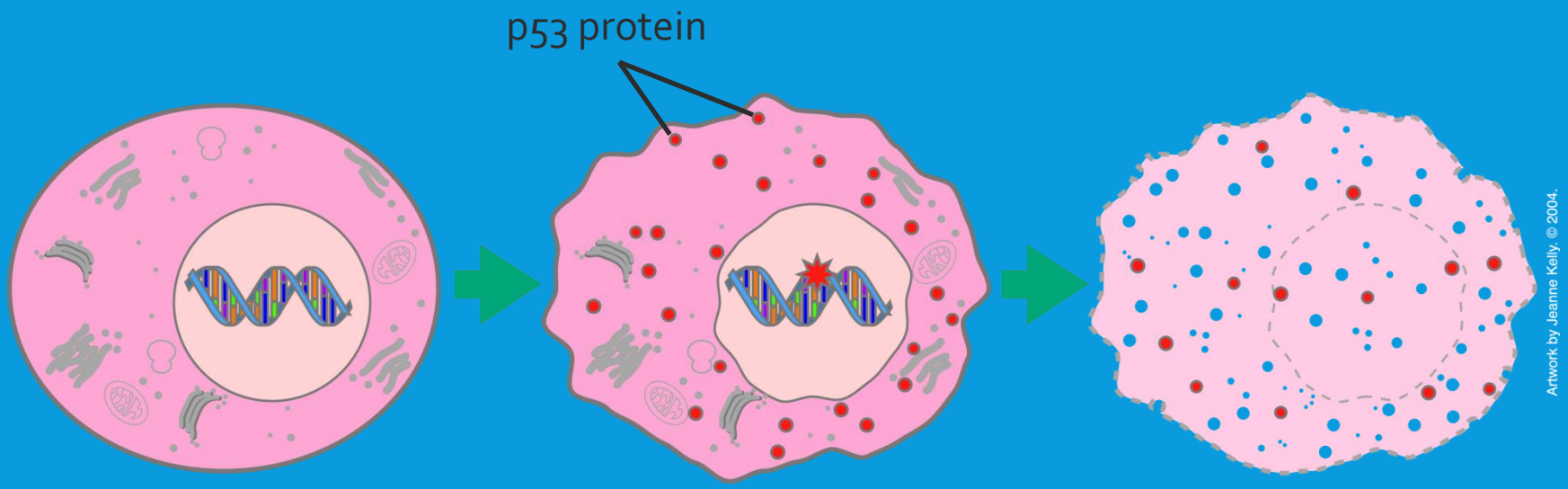
WHAT IS THE DIFFERENCE BETWEEN PROTO-ONCOGENES AND TUMOR SUPPRESSOR GENES

- **Proto-oncogenes** function as regulators of cell growth
- **Proto-oncogenes** have a role in DNA repair
- **Proto-oncogenes** are normal genes essential for normal cell growth
- **Tumor suppressor genes** function as regulators of cell growth
- **Tumor suppressor genes** are a type of repair gene

Tumor Suppressor Genes Act Like a Brake Pedal



P53 Tumor Suppressor Protein Triggers Cell Suicide



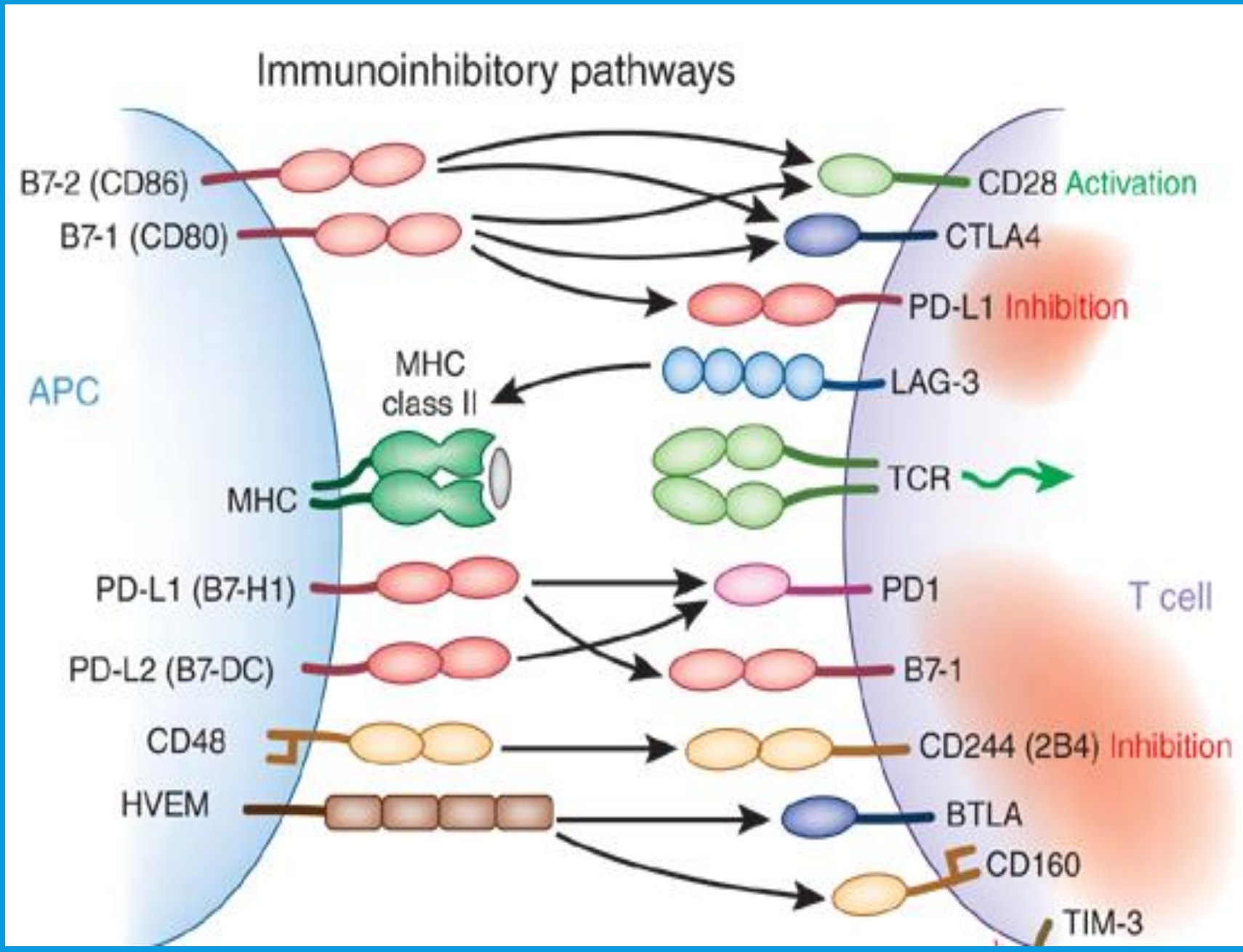
Normal cell

Excessive DNA damage

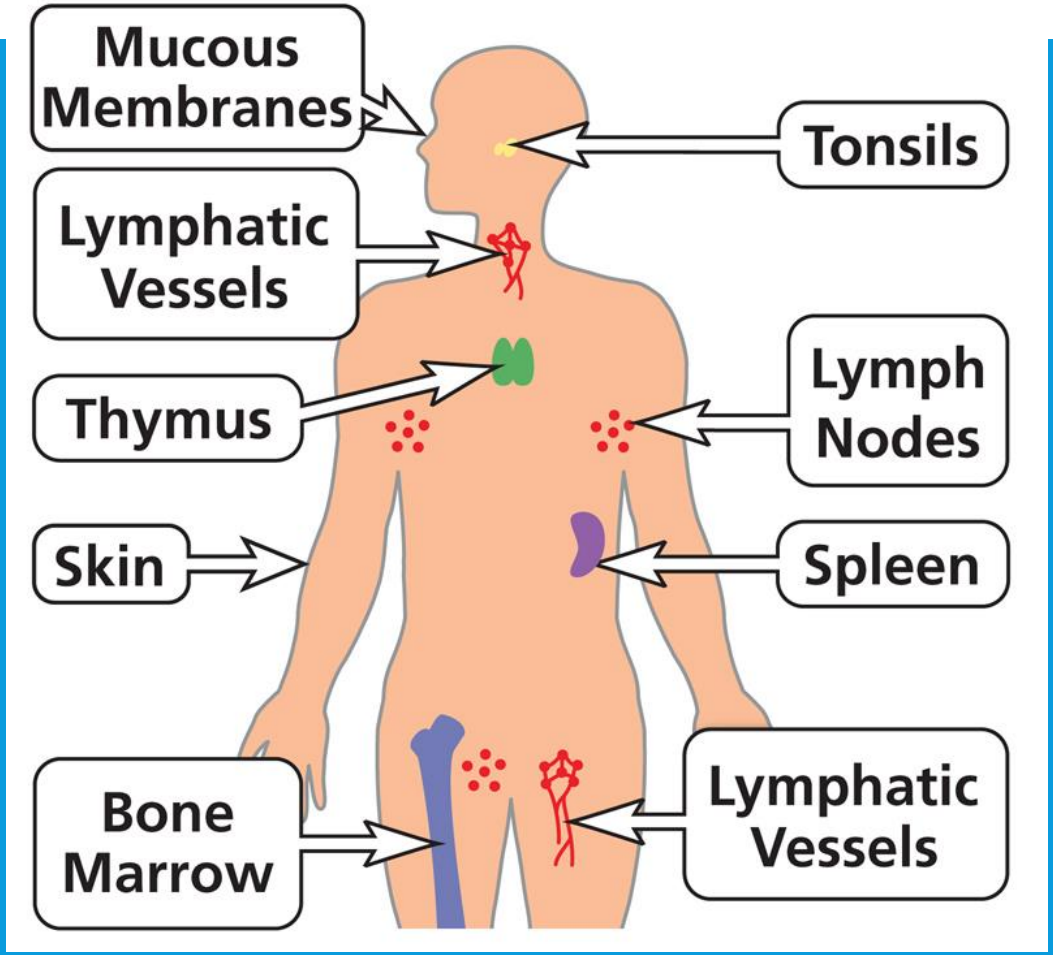
Cell suicide
(Apoptosis)

IMMUNE SURVEILLANCE

- As tumor cells differentiate, they produce proteins or antigens expressed on the cell surface
- Immune system recognizes these cells as non-self
- An immune response is mounted in defense
- Through a variety of mechanisms, the immune system destroys the foreign/non-self object (NK cells, cytotoxic T Cells, etc.)
- Tumors can develop if they evade Immune surveillance


Immunoinhibitory pathways
B7-2 (CD86)
B7-1 (CD80)
CD28 Activation
CTLA4
PD-L1 Inhibition
APC
MHC class II
LAG-3
MHC
TCR
PD-L1 (B7-H1)
PD1
T cell
PD-L2 (B7-DC)
B7-1
CD48
CD244 (2B4) Inhibition
HVEM
BTLA
CD160
TIM-3

Immune System



DETECTION

- Screening
- Symptoms
- Happenstance

SCREENING

- Identify asymptomatic persons worth risk factors for a disease
- Detect occult disease
- Direct patients to genetic counseling
- Reassurance

ATTRIBUTES OF SCREENING

- Sensitivity
- Specificity predicative
- Safe
- Easy
- Convenient
- Cost effective

EVIDENCE BASED SCREENING

- National Comprehensive Cancer Network (NCCN)
- American Cancer Society (ACS)
- National Cancer Institute (NCI)
- American College of Obstetricians and Gynecologists(AGOC)

SCREENING GUIDELINES- AMERICAN CANCER SOCIETY

- Colorectal
- Skin
- Breast
- Cervical
- Testicular
- Prostate
- Lung

SCREENING EXAMPLES

- Radiological (Mammography)
- Clinical Laboratory Testing (Pap Smears, Fecal Occult Blood Tests, PSA Test)
- Procedural (Colonoscopy, Sigmoidoscopy)
- Physical Exam (BSE/TSE, clinical breast/testicular exam, Digital Rectal Exam)

BREAST CANCER

- Women ages 40 to 44 should have the choice to start annual breast cancer screening with mammograms (x-rays of the breast) if they wish to do so.
- Women aged 45 to 54 should get mammograms every year.
- Women 55 and older should switch to mammograms every 2 years or can continue yearly screening.
- Screening should continue if a woman is in good health and is expected to live 10 more years or longer.
- All women should be familiar with the known benefits, limitations, and potential harms linked to breast cancer screening. They also should know how their breasts normally look and feel and report any breast changes to a health care provider right away.

PROSTATE CANCER

- The American Cancer Society recommends that men make an informed decision with a health care provider about whether to be tested for prostate cancer.
- Research has not yet proven that the potential benefits of testing outweigh the harms of testing and treatment.
- It is believed that men should not be tested without first learning about what is known and unknown about the risks and possible benefits of testing and treatment.
- Starting at age 50, men should talk to a health care provider about the pros and cons of testing so they can decide if testing is the right choice for them.
- If an African American male has a father or brother who had prostate cancer before age 65, they should have this talk with a health care provider starting at age 45.
- If the decision to be tested is made, the individual should get a PSA blood test with or without a rectal exam.
- How often one is tested will depend on the PSA level

LUNG CANCER

- The American Cancer Society does not recommend tests to check for lung cancer in people who are at average risk. There are screening guidelines for those who are at high risk of lung cancer due to cigarette smoking. Screening might be right if an individual have all of the following:
- 55 to 74 years of age
- In good health
- Have at least a 30 pack-year smoking history AND are either still smoking or have quit within the last 15 years (A pack-year is the number of cigarette packs smoked each day multiplied by the number of years a person has smoked. Someone who smoked a pack of cigarettes per day for 30 years has a 30 pack-year smoking history, as does someone who smoked 2 packs a day for 15 years.)
- Screening is done with an annual low-dose CT scan (LDCT) of the chest. If you fit the list above, talk to a health care provider if you want to start screening.

WHEN TO LOOK CLOSER

- Change in bowel/bladder habits
- Unusual bleeding/discharge
- Sore that doesn't heal
- Mole or wart change
- Thickening or lump
- Nagging cough or hoarseness
- Indigestion/swallowing difficulty

FOUND SOMETHING, WHAT NOW?

LAB

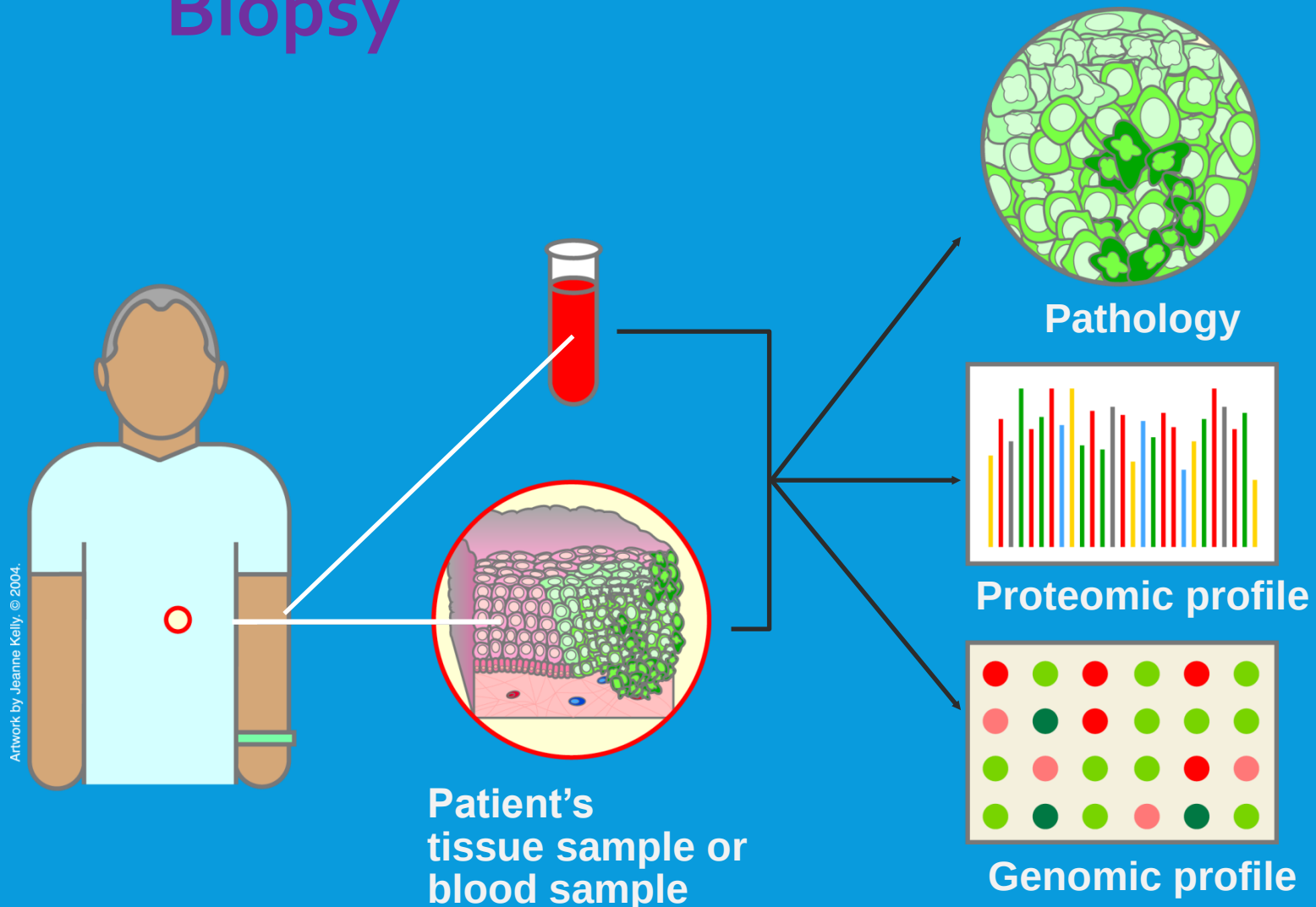
IMAGING

INVASIVE PROCEDURES

LABORATORY INVESTIGATIONS

- Hematology studies
- Chemistry studies
- Radioimmunoassay
  - Tumor markers
    - Enzymes
    - Hormones
    - Metabolic products
    - Proteins
    - antigens
- Flow cytometry
  - DNA
  - Cell surface markers

Biopsy


Artwork by Jeanne Kelly. © 2004.
Patient's
tissue sample or
blood sample
Pathology
Proteomic profile
Genomic profile

PATHOLOGY

- Cytogenetics

- INDICATION FOR TEST: Gastrointestinal Tract (Colon) Adenocarcinoma, Signet-Ring Cell Type Metastatic to Hematopoietic and Lymphoid Tissue (Lymph Node)

  SPECIMEN(S) TESTED: S15-35344 A2 (Massachusetts General Hospital, Boston, MA, United States)

  RESULTS:
  Targeted RNA next generation sequencing (NGS) using Anchored Multiplex PCR (AMP) detected no fusion transcripts in ALK, RET, and ROS1.

  INTERPRETATION:

  NEGATIVE for ALK, RET, and ROS1 rearrangement.

  TEST INFORMATION:
  We have developed Anchored Multiplex PCR (AMP) for targeted fusion transcript detection using next generation sequencing (NGS) [1]. Briefly, total nucleic acid was isolated from a formalin-fixed paraffin embedded tumor specimen after histological review for tumor enrichment. The total nucleic acid was reverse transcribed with random hexamers, followed by second strand synthesis to create double-stranded complementary DNA (cDNA). The double-stranded cDNA was end-repaired, adenylated, and ligated with a half-functional adapter. Two hemi-nested PCR reactions were applied to create a fully functional sequencing library that targets specific genes (exons) listed below. Illumina MiSeq 2 x 147 base pair paired-end sequencing results were aligned to the hg19 human genome reference using bwa-mem [2]. A laboratory-developed algorithm was used for fusion transcript detection and annotation. The integrity of the input nucleic acid and the technical performance of the assay were assessed with a qualitative reverse transcription qPCR assay and assessing the DNA/RNA content in the sequencing results. Although this assay may detect several potential fusion variants, only the most prevalent one is reported. The assay is validated for samples showing 20% or higher tumor cellularity and for clinical reporting of fusion transcripts involving ALK, RET, and ROS1.

SNAPSHOT

- TARGETED GENES (EXONS):

ADCK4 (1-2, 4-6, 9-10, 12-15), AKT3 (1-2, 13), ALK (1,3, 17, 19-22, 29), AR (1-4, 6, 7-8), ARHGAP6 (1-3), ARHGAP26 (10-13), AXL(14-15), BRAF (1-2, 8-11, 17), BRD4 (1, 10-12), CCDC6 (1-8), CD74 (1-8), CHTOP(2- 6), EGFR (7-9, 14-18, 23-28), ERBB2 (2-4), ERBB4 (17-18, 20), ESR1 (3-5),EWSR1 (1, 3-8, 12-13), FGFR1 (1, 7-13, 16-18), FGFR2 (3-4, 17), FGFR3 (3, 7-12,15-18), FGR (2-3), INSR (13-18, 21-22), INSRR (13-18, 21-22), JAK1 (1-7, 9-25),JAK2 (1, 6, 9, 11-12, 16-17, 19, 24), MAML2 (2-4), MAST1 (2, 8, 19-20, 26, 29),MAST2 (1, 5), MET (2, 11-16, 20-21), MUSK (8-9, 11-14), NFIB (1, 7-9), NOTCH1(2, 27-28, 34), NOTCH2 (1, 27, 33), NRG1 (2-4, 6), NTRK1 (1, 8-17), NTRK2 (9-11,13-20), NTRK3 (1, 11-16, 18 19), NUMBL (3-7, 9-10), NUTM1 (2-3), PDGFB (1-2, 6),PDGFRA (1, 9-11, 13-14, 20-23), PIK3CA (2-3), PKN1 (9-14), PLAG1 (2-4), PPARG(3-8), PRKACA (2-4), PRKCA (3-7), PRKCB (3-7), RAF1 (1, 9-11, 17), RET (1, 8-13,19), RHOA (1-5), ROS1 (1, 31-37, 43), TMPRSS2 (1-5).

TARGETED THERAPY

- TARGETED GENES (EXONS):

ADCK4 (1-2, 4-6, 9-10, 12-15), AKT3 (1-2, 13), ALK (1, 3, 17, 19-22, 29), AR (1-4, 6, 7-8), ARHGAP6 (1-3), ARHGAP26 (10-13), AXL(14-15), BRAF (1-2, 8-11, 17), BRD4 (1, 10-12), CCDC6 (1-8), CD74 (1-8), CHTOP (2- 6), EGFR (7-9, 14-18, 23-28), ERBB2 (2-4), ERBB4 (17-18, 20), ESR1 (3-5), EWSR1 (1, 3-8, 12-13), FGFR1 (1, 7-13, 16-18), FGFR2 (3-4, 17), FGFR3 (3, 7-12,15-18), FGR (2-3), INSR (13-18, 21-22), INSRR (13-18, 21-22), JAK1 (1-7, 9-25),JAK2 (1, 6, 9, 11-12, 16-17, 19, 24), MAML2 (2-4), MAST1 (2, 8, 19-20, 26, 29),MAST2 (1, 5), MET (2, 11-16, 20-21), MUSK (8-9, 11-14), NFIB (1, 7-9), NOTCH1(2, 27-28, 34), NOTCH2 (1, 27, 33), NRG1 (2-4, 6), NTRK1 (1, 8-17), NTRK2 (9-11,13-20), NTRK3 (1, 11-16, 18-19), NUMBL (3-7, 9-10), NUTM1 (2-3), PDGFB (1-2,6),PDGFRA (1, 9-11, 13-14, 20-23), PIK3CA (2-3), PKN1 (9-14), PLAG1 (2-4), PPARG(3-8), PRKACA (2-4), PRKCA (3-7), PRKCB (3-7), RAF1 (1, 9-11, 17), RET (1, 8-13,19), RHOA (1-5), ROS1 (1, 31-37, 43), TMPRSS2 (1-5).

TUMOR MARKERS

Biological substances used to guide and monitor treatment and potential disease activity

- **CEA (carcinoembryonic antigen)**
  - Bladder, breast, colon, lung, ovarian, pancreatic, stomach, thyroid cancers
- **PSA (prostate specific antigen)**
  - Prostate
- **CA-125 (cancer antigen 125)**
  - Ovarian cancer
- **CA 27-29**
  - Breast, colon, stomach, kidney, lung, ovarian, pancreas, uterus, liver cancers
- **AFP (alfa fetoprotein)**
  - Liver cancer, non-seminomatous germ cell tumors

IMAGING

X-ray

- Lung
- Surveillance/initial detection

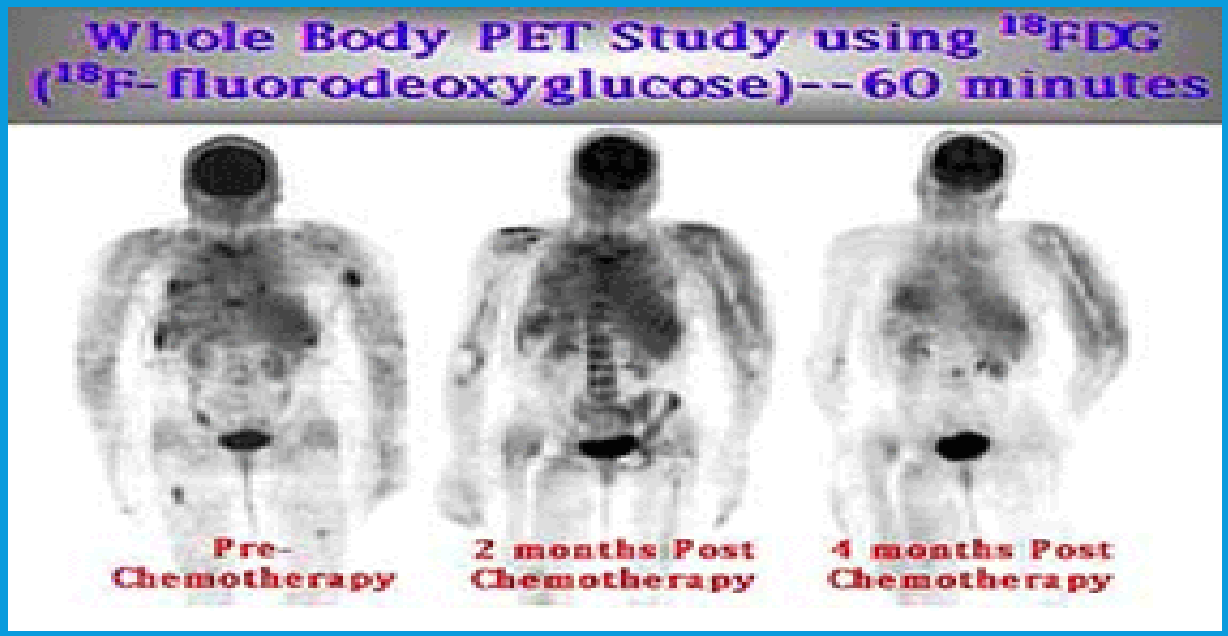
PET

- Benign/malignant
- Guidance for bx

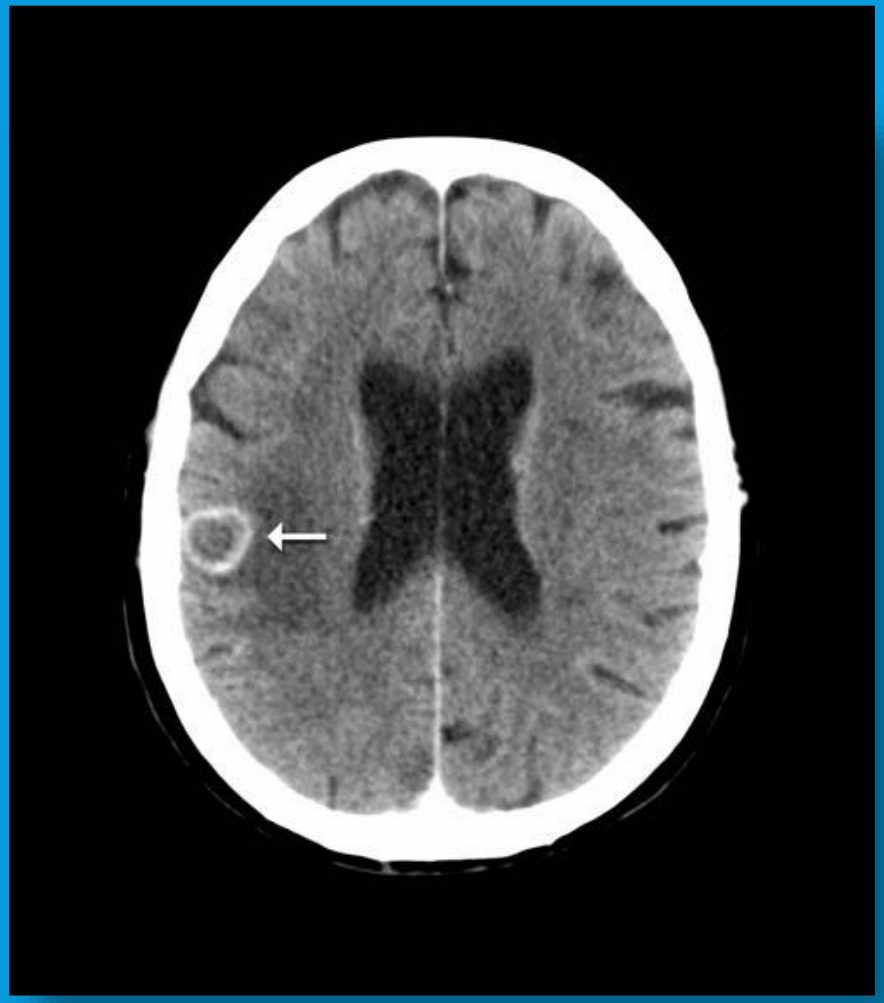
MRI

CT scans

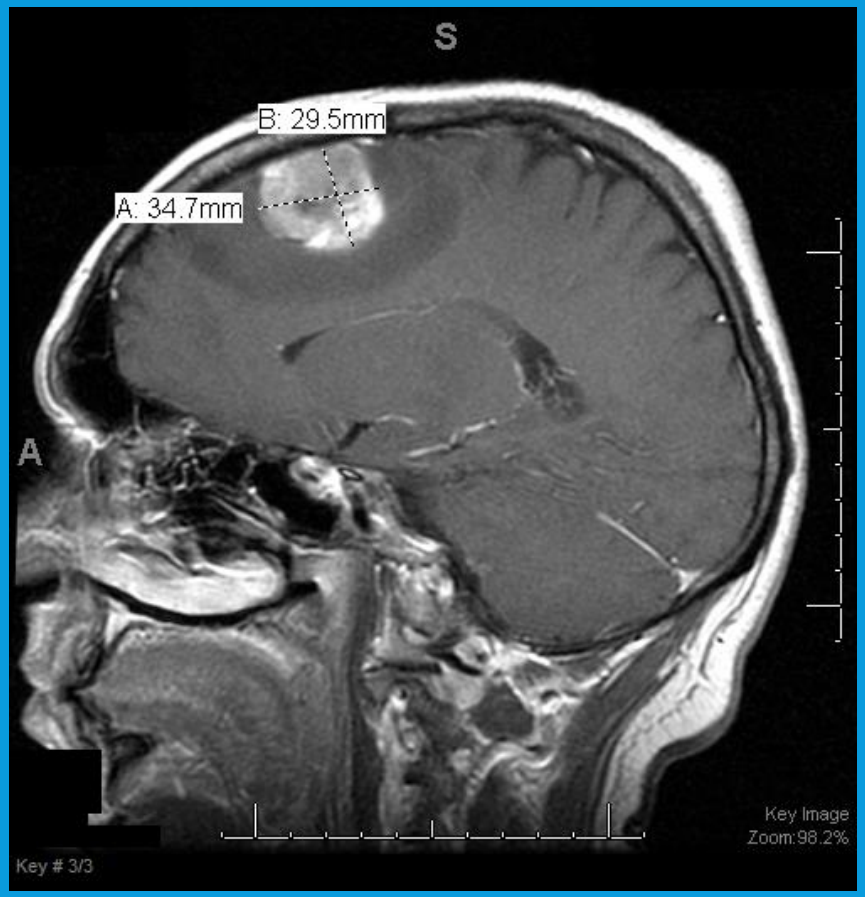
PET CT (POSITRON EMISSION TOMOGRAPHY)



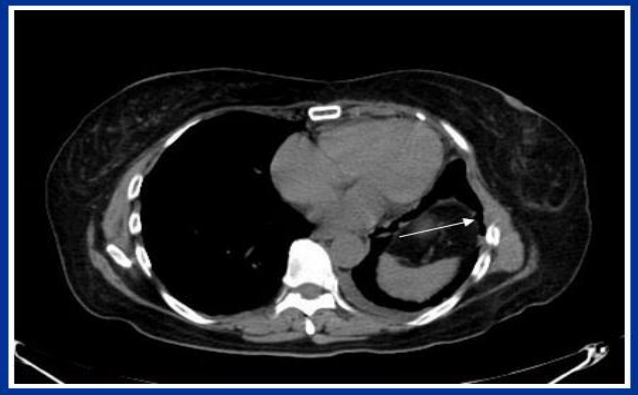
CT SCAN

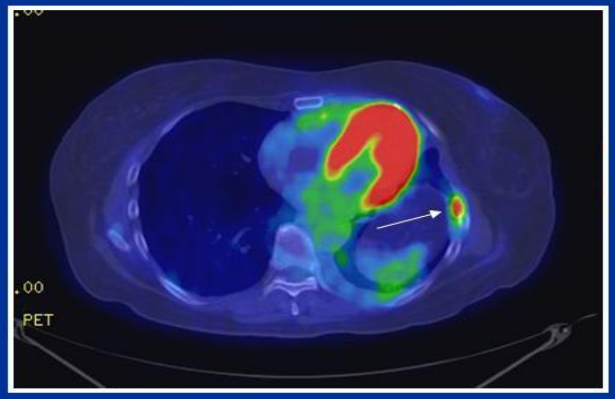


MAGNETIC RESONANCE IMAGE



CT alone, and PET/CT Fusion





PET avid
pleural nodules

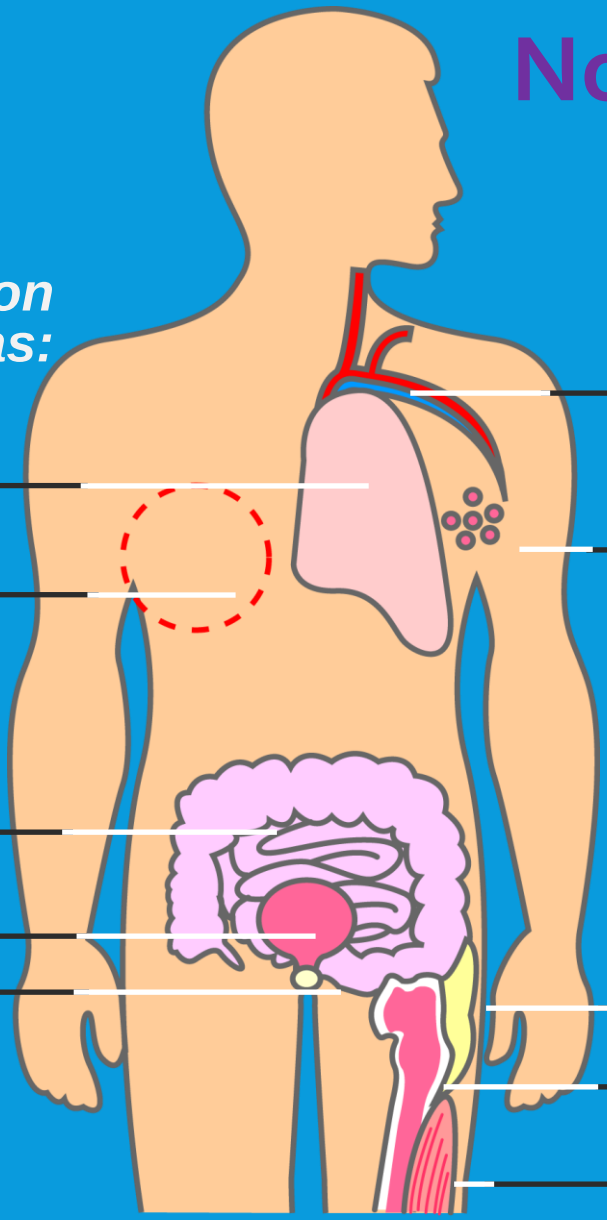
INVASIVE PROCEDURES

- Endoscopy
- Biopsy
  - Surgical
    - Excisional
    - incisional
  - Needle
    - FNA
    - Core
    - Vacuum

TUMOR NOMENCLATURE

- Tissue of Origin
- Benign vs. malignant
- Solid
  - Epithelial
  - Mesenchymal
  - Neural
  - mixed
- Hematologic

Nomenclature



Artwork by Jeanne Kelly. © 2004.

Some common carcinomas:

- Lung
- Breast (women)
- Colon
- Bladder
- Prostate (men)

Leukemias:

- Bloodstream

Lymphomas:

- Lymph nodes

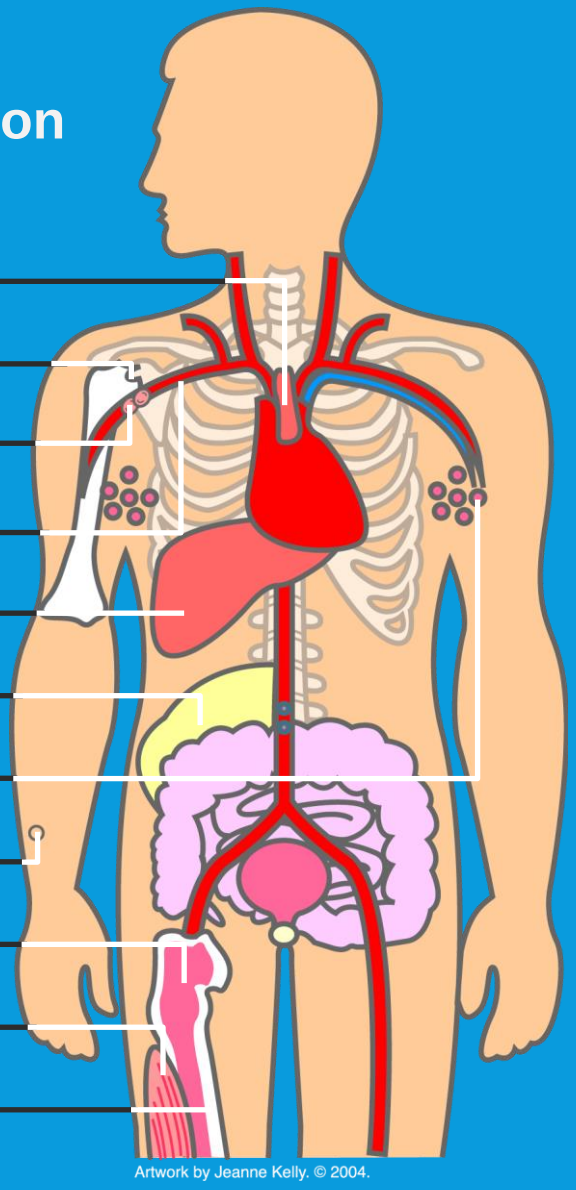
Some common sarcomas:

- Fat
- Bone
- Muscle

Nomenclature

Cancer Prefixes Point to Location

Prefix	*Meaning*
adeno-	gland
chondro-	cartilage
erythro-	red blood cell
hemangio-	blood vessels
hepato-	liver
lipo-	fat
lympho-	lymphocyte
melano-	pigment cell
myelo-	bone marrow
myo-	muscle
osteo-	bone



GRADING AND STAGING – WAYS TO CHARACTERIZE TUMOR GROWTH AND PROGNOSIS

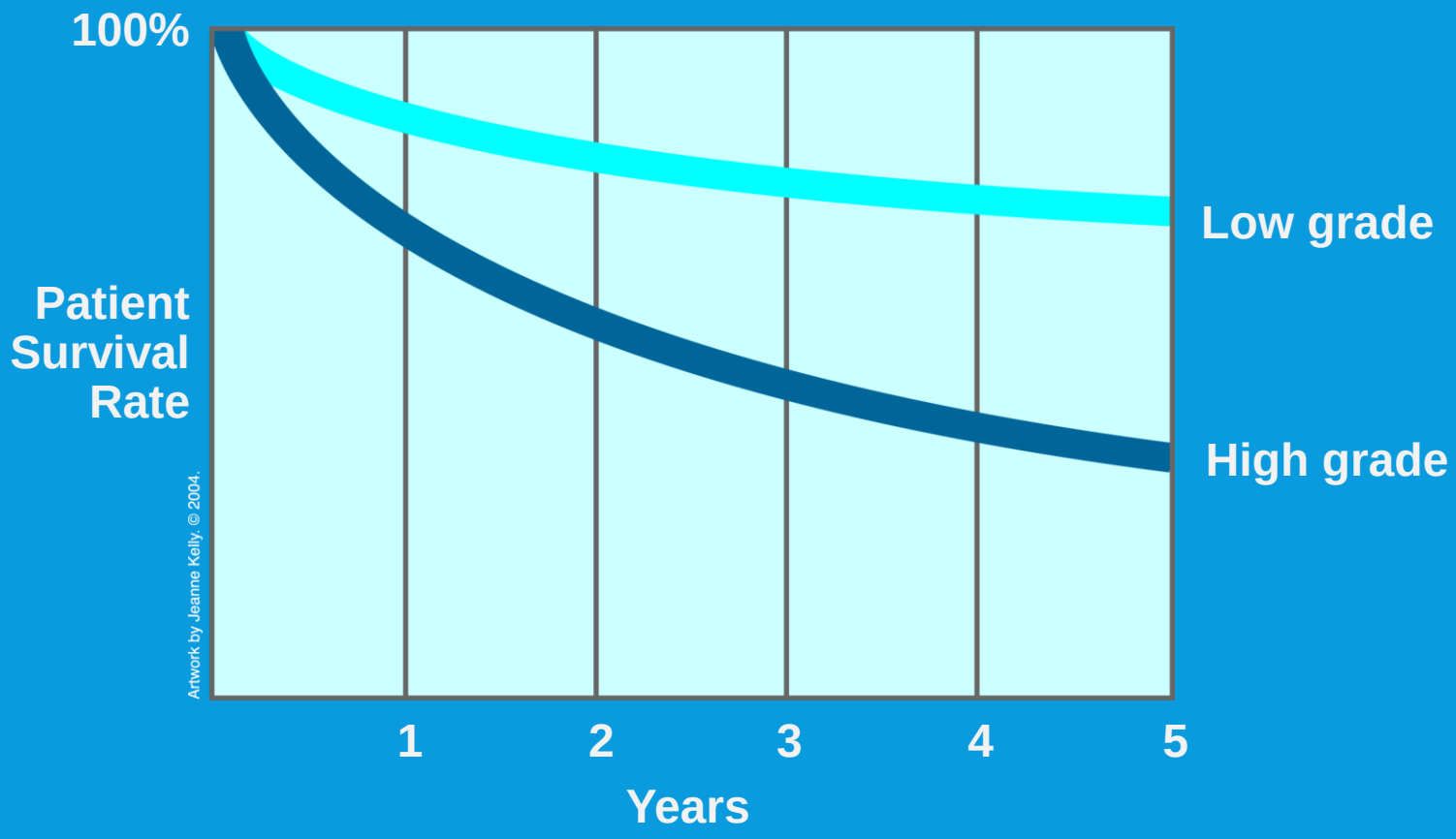
- Grading – Degree of cell dedifferentiation
- Anatomic Staging – Degree of spread
  - TNM System-The Gold Standard

TUMOR GRADING

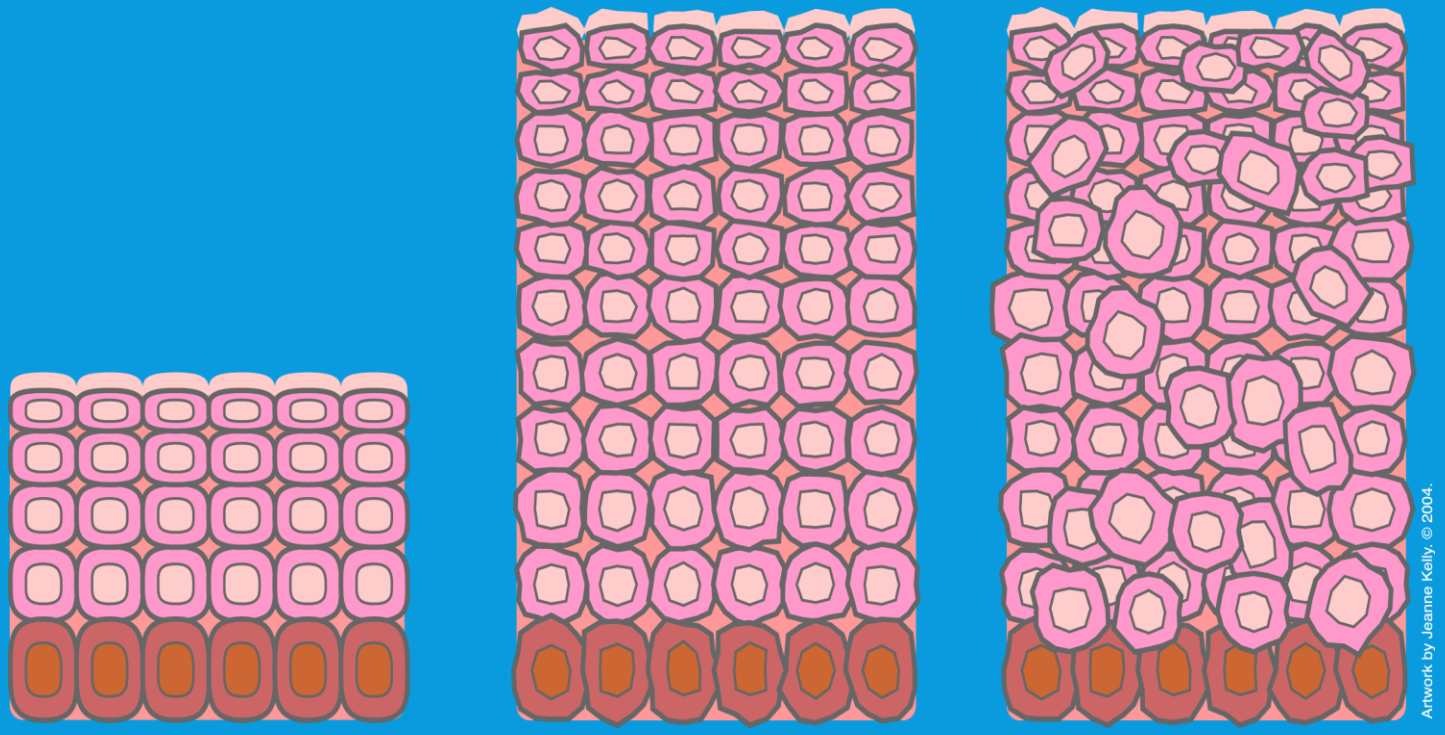
- GX - undetermined
- G1 – well differentiated, low grade
  - strong resemblance to parent cell
- G2 – moderately differentiated, intermediate grade
- G3 – poorly differentiated, high grade
- G4 – undifferentiated, high grade
  - impossible to tell parent cell

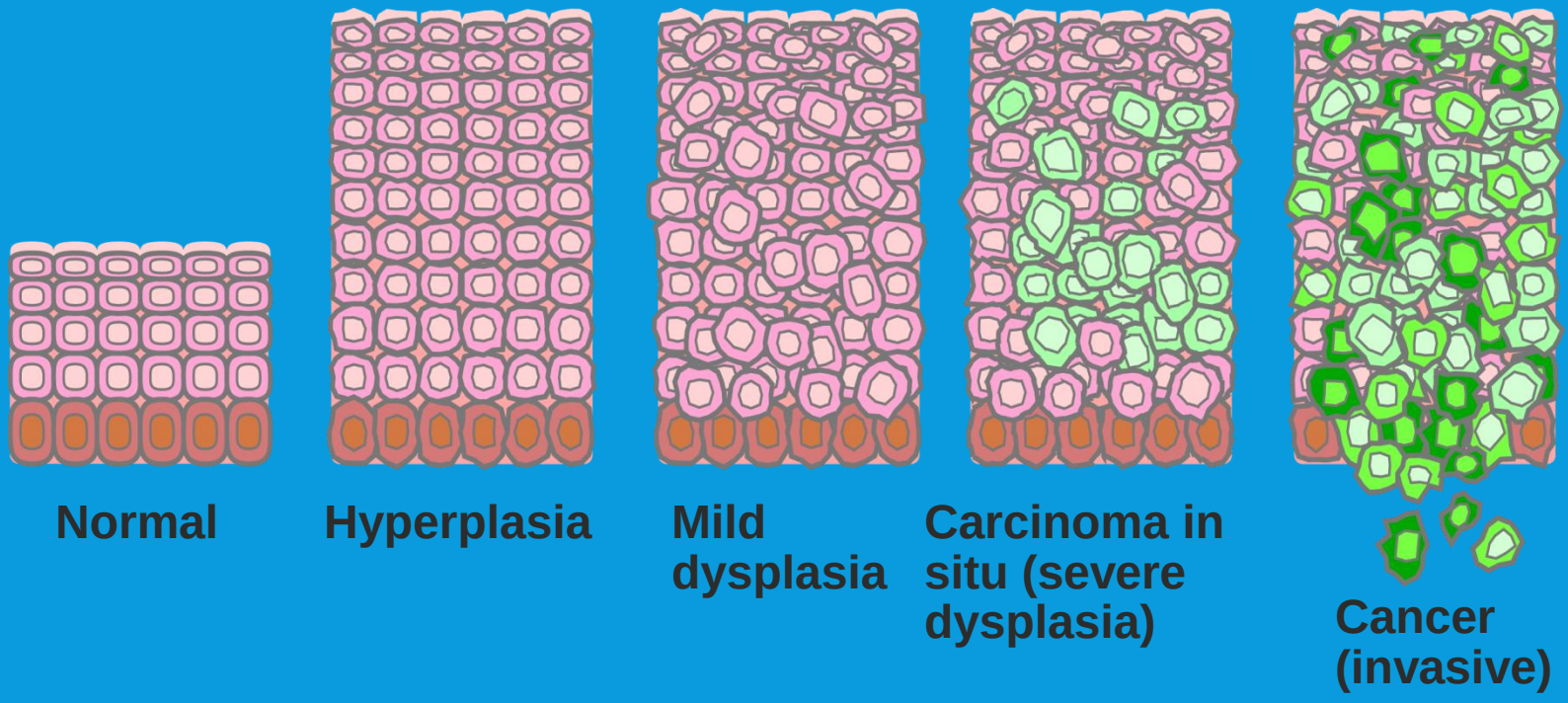
Tumor Grading

General Relationship Between Tumor Grade and Prognosis



Dysplasia


Normal
Hyperplasia
Mild dysplasia
Artwork by Jeanne Kelly. © 2004.


Normal
Hyperplasia
Mild dysplasia
Carcinoma in situ (severe dysplasia)
Cancer (invasive)
Artwork by Jeanne Kelly. © 2004.

POLL QUESTION:

Which of the following represents a high grade, poorly differentiated tumor?

1. Grade I
2. Grade II
3. Grade III
4. Grade IV

STAGING

- Solid Tumors
- Hematologic Malignancies

TNM STAGING SYSTEM

- Determination of how extensive the malignancy is -
  - **T** = tumor size (also depth of invasion)
  - **N** = nodal status (number and location of positive Lymph Node)
  - **M** = metastatic disease

STAGING

- **Solid**
  - 0 – 4
  - Clark/Breslow – Melanoma
  - Dukes - Colon
- **Hematologic**
  - Ann Arbor – NHL
  - TNM doesn't fit

TNM STAGING

Stage 0	Tis	N0	M0
Stage 1A	T1	N0	M0
Stage 1B	T1	N1	M0
	T2	N0	M0
Stage II	T1	N2	M0
	T2	N1	M0
	T3	N0	M0
Stage IIIA	T2	N2	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T3	N2	M0
	T4	N1	M0
Stage IV	T4	N2	M0
	Any T	Any N	M1

STAGING OF HEMATOLOGIC MALIGNANCIES

- Lymphoma
- Leukemia
- Multiple Myeloma

TUMOR PATHOLOGY

- Tissue of origin
- Biological behavior
- Cell differentiation
- Hetero- vs. Homogeneity
- Mitotic count
- Vascularization
- Lymphatic invasion

PREVENTION AND EARLY DETECTION

- The key to improving outcomes and survival
- Availability of preventative measures and resources for early detection is limited in developing countries.

PREVENTION

- Screening
- Risky behavior modification
- Nutrition
- Chemoprevention

CANCER PREVENTION

Avoid	Avoid Tobacco
Limit	Limit Alcohol and Tobacco
Consume	Consume Fruits and Vegetables
Limit	Limit Fats and Calories
Protect	Protect Yourself From Excessive Sunlight
Avoid	Avoid Cancer Viruses
Avoid	Avoid Carcinogens at Work

Nutrition and Physical Activity Guidelines for Cancer Prevention

For the great majority of Americans who do not use tobacco, weight control, dietary choices, and levels of physical activity are the most important modifiable determinants of cancer risk. The American Cancer Society guidelines reflect the most current scientific evidence related to dietary and activity patterns and cancer risk. They focus on recommendations for individual choices but also present recommendations for community action to create a supportive social and physical environment in which individuals have genuine opportunities to choose healthy behaviors.

American Cancer Society Nutrition and Physical Activity Guidelines for Cancer Prevention (2012)

Full text of current ACS guidelines on nutrition and physical activity for cancer prevention is available here.

Quick Look: Chart of American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention

View a summary chart of current ACS recommendations for individual choices and community action.

For Your Patients: ACS Guidelines on Nutrition and Physical Activity for Cancer Prevention

Review a consumer-friendly version of the American Cancer Society's nutrition and physical activity guidelines for cancer prevention.

Stay Healthy Topics

- Stay Away from Tobacco
- Eat Healthy and Get Active
- Be Safe in the Sun
- Other Ways to Protect Yourself
- Find Cancer Early
- ACS Programs to Help You Stay Well
- Tools and Calculators
- Information for Health Care Professionals


CAMEL
Smoking can damage the sperm and decreases fertility
CAMEL
Smoking kills
€34.50
0
Winston
Smoking kills
€73.00

WHY ARE CANCER CLINICAL TRIALS IMPORTANT?

- Clinical trials translate results of basic scientific research into better ways to prevent, diagnose, or treat cancer
- The more people that take part, the faster we can:
  - Answer critical research questions
  - Find better treatments and ways to prevent cancer

WHY ARE CANCER CLINICAL TRIALS IMPORTANT?

- Cancer Site Compare statistics for selected cancer sites.
- Race/Sex Compare cancer statistics by both race and sex.
- Race/Ethnicity Compare cancer statistics by race or by the expanded race/ethnicity groupings.

WHY ARE CANCER CLINICAL TRIALS IMPORTANT?

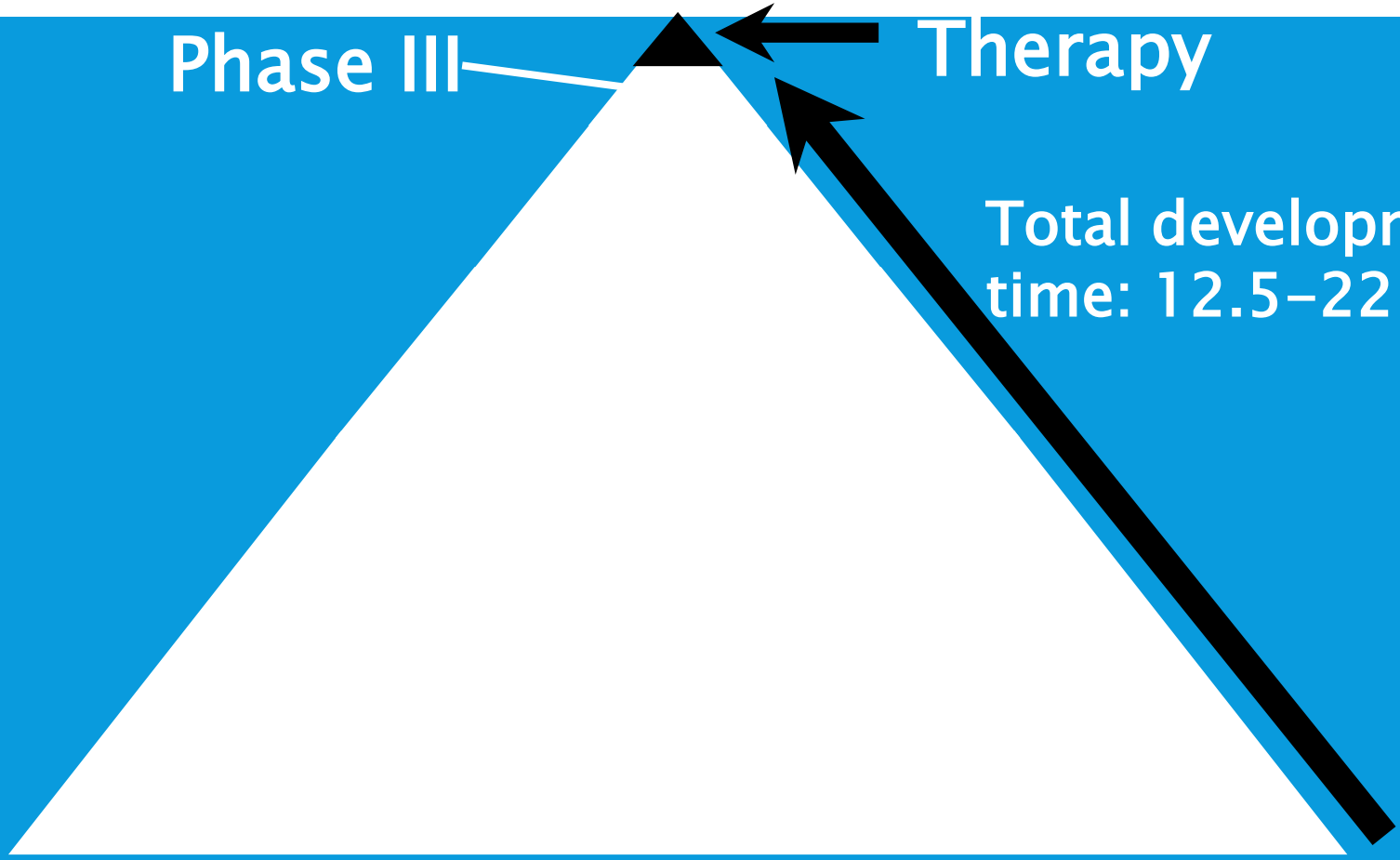
- Age at Diagnosis/Death Compare statistics by age groups for a selected cancer site, race, and sex.
- Sex Compare the differences between male and female cancer statistics.
- Data Type Compare Incidence, Delay-adjusted Incidence and Mortality cancer statistics.

TYPES OF CANCER CLINICAL TRIALS

- Treatment trials
- Prevention trials
- Early-detection trials/screening trials
- Diagnostic trials
- Quality-of-life studies/supportive care studies

CLINICAL TRIAL "SPONSORS"

- Cooperative Groups
- Pharmaceutical Companies
- Investigator Initiated


Phase III
Therapy
Total development time: 12.5-22 yrs.

CLINICAL TRIAL PHASES

Phase 1 trials (*helpful hint - What Dose?*)

- How does the agent(s) affect the human body?
- What dosage is safe?
- Subjects on these trials are assigned to a designated dose level of the drug(s) at the time of enrollment

Phase 1

Purpose:

To find a safe dose
To decide how the new treatment should be given (by mouth, in a vein, etc.)
To see how the new treatment affects the human body and fights cancer

Number of people taking part: from 20-80 participants

CLINICAL TRIAL PHASES

Phase 2 trials (*helpful hint – What Disease?*)

- Does the agent or intervention have an effect on the cancer?
- Patients enrolled in this phase trial share same tumor type and/or stage of disease

Phase 2

Purpose:

To determine if the new treatment has an effect on a certain cancer
To see how the new treatment affects the body and fights cancer

Number of people taking part: from 100 – 300 participants

CLINICAL TRIAL PHASES

Phase 3 trials (*helpful hint - Is it better?*)

- Is the new agent or intervention (or new use of a treatment) better than the standard?
- Rare to have a placebo alone arm in a cancer treatment trial

Phase 3

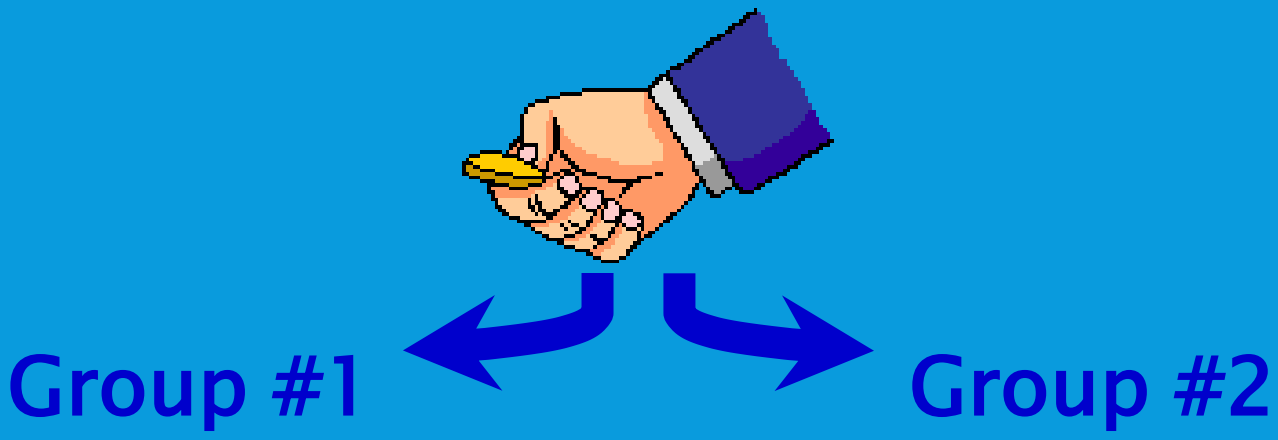
Purpose:

To compare the new treatment (or new use of a treatment) with the current standard treatment

Number of people taking part: from 300 to 3000 participants

TREATMENT DEVELOPMENT

- **Phase 3 Trials**
  - Randomly assigned to one of two (or more) groups



WHY IS RANDOMIZATION IMPORTANT?

So, all groups are as alike as possible

Provides the best way to prove the effectiveness of a new agent or intervention

ROLES OF THE CLINICAL RESEARCH NURSE

- Advocate - human subject protection
- Support the informed consent process
- Regulatory specialist, collect data
- Care coordination and continuity with the research team
- Clinician – direct care provider, study coordinator, advanced clinician

JASON CARTER
CLINICAL TRIALS PROGRAM

NATIONAL CANCER INSTITUTE
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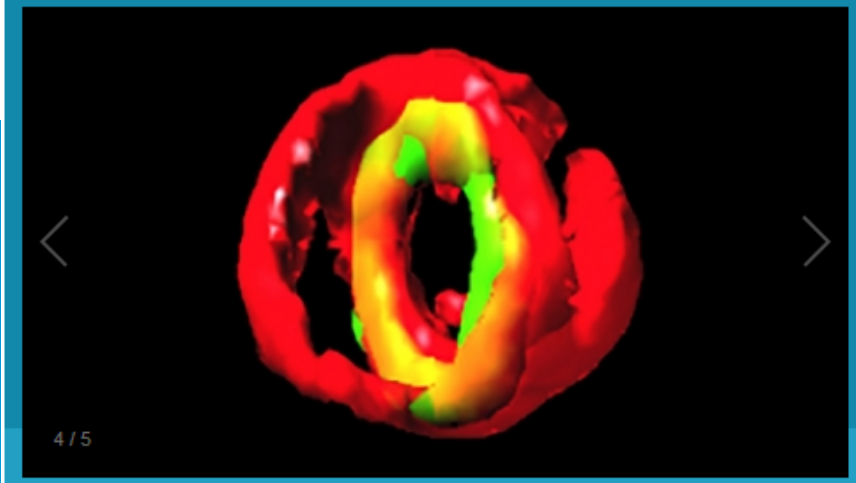

Study reveals function of protein crucial to survival of Staph infections

Read more...

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#WhyIFightFlu "It's pretty amazing how 5 seconds of my time can protect so many folks for months to come!"... https://t.co/vGADak0YrJ

NCI Center for Cancer Research @NCIResearchCtr

RT @NCICancerTrials: In this clip, Jennie Lucca of @TheChildrensInn describes the services The Inn

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EVIDENCE BASED RESOURCES

- American Cancer Society: www.cancer.org
- American Society of Clinical Oncology (ASCO): http://www.asco.org/portal/site/ASCO
- International Association of Clinical Research Nurses (IACRN): www.iacrn.org
- National Cancer Institute: www.cancer.gov
- National Comprehensive Cancer Network (NCCN): www.nccn.org
- Oncology Nursing Society: www.ons.org
- Seer's Training: www.training.seer.cancer.gov

POLL QUESTION:

Phase 1 clinical trials primary objective is curative.

1. True
2. False

POLL QUESTION:

Phase 2 clinical trials primary objective is efficacy of the medication or treatment.

1. True
2. False

POLL QUESTION:

Phase 3 clinical trials randomize patient to test the new medication or treatment compared to the standard of treatment.

1. True
2. False

Which of the following represents a high grade, poorly differentiated tumor?


BOSTON ONCOLOGY NURSING SOCIETY
BONS


ONS®
Oncology Nursing Society