Neoplasia

Nature of Cancer

Cancer Genes

Treating Cancer

CANCER _ definition

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.
Cancer can start almost **anywhere** in the human body, which is made up of trillions of cells.

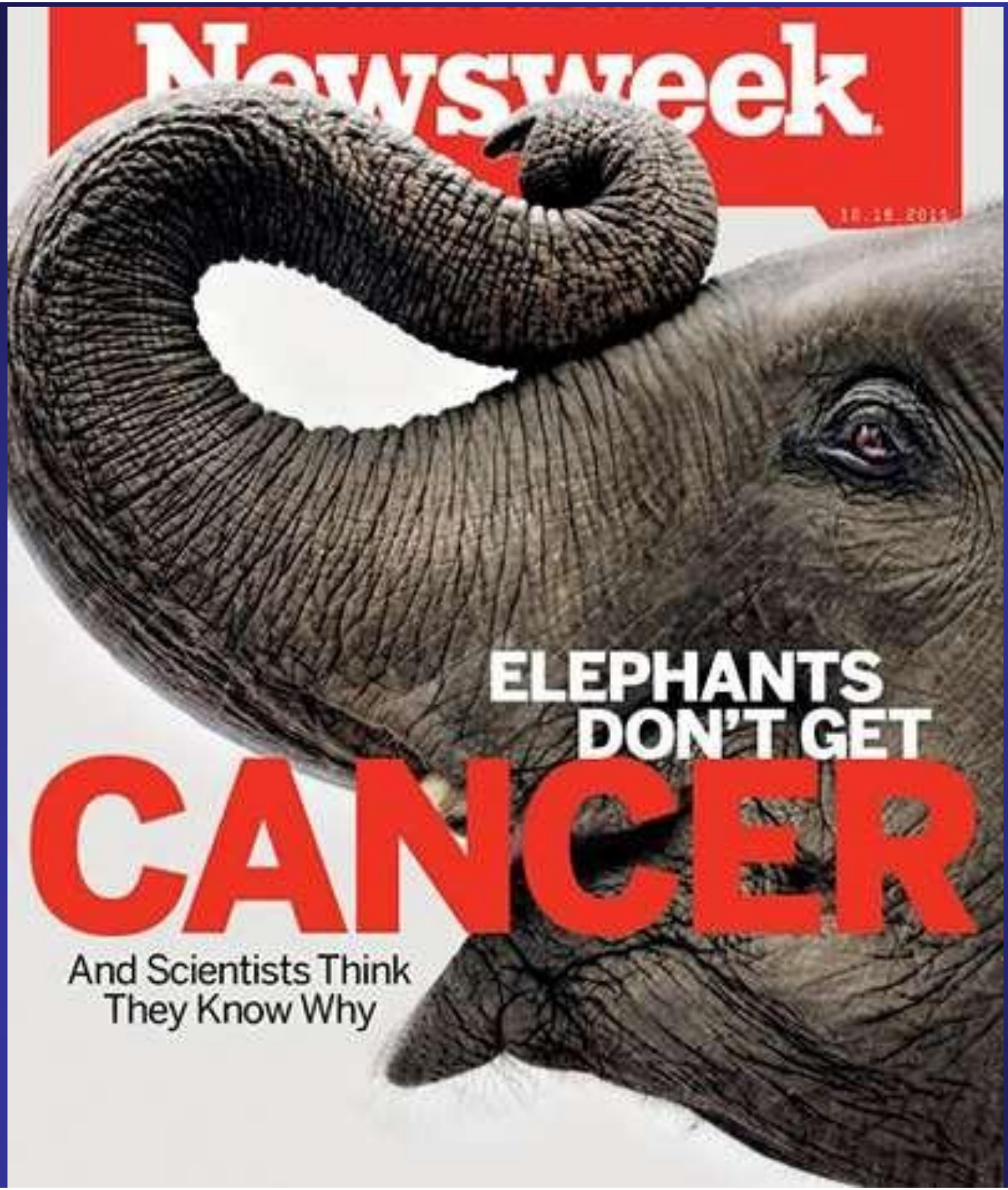
Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place.

Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't.
These cells may form tumors, which are lumps of tissue.

https://www.cancer.gov/about-cancer/understanding/what-is-cancer#definition

Cancer in dinosaurs

Lancet oncology 2020, Aug;21(8):1021-1022


Newsweek
ELEPHANTS DON'T GET
CANCER
And Scientists Think They Know Why

Gene Quantity in Cancer

HUMANS vs. ELEPHANTS

JAMA. 2015;314(17):1850-1860

Why Elephants are resistant to cancer?

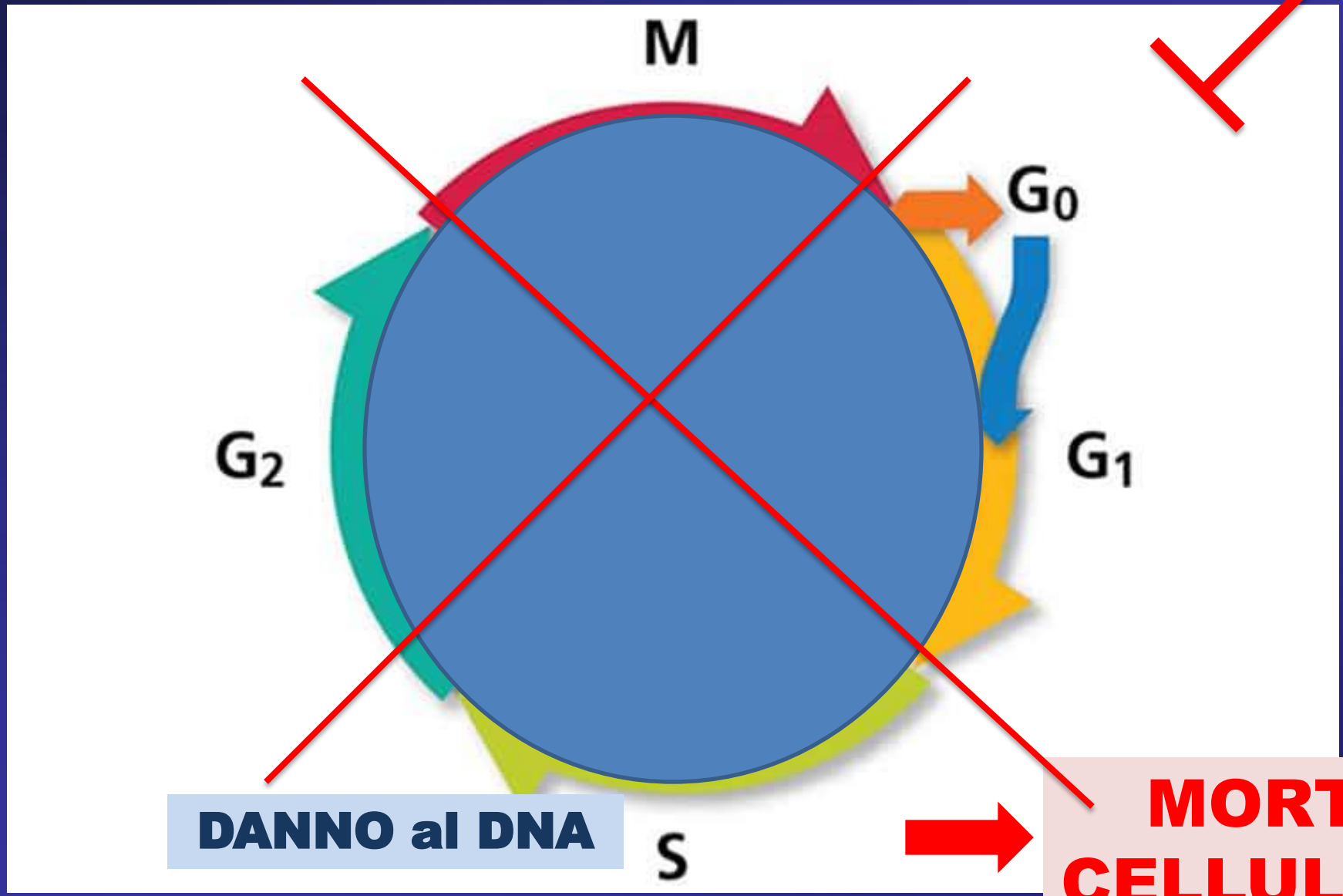
In risposta ad un DANNO del DNA

Le cellule di elefante vanno incontro a apoptosi (morte cellulare) mediata dalla proteina p53

Con una frequenza più elevata rispetto alle cellule di uomo

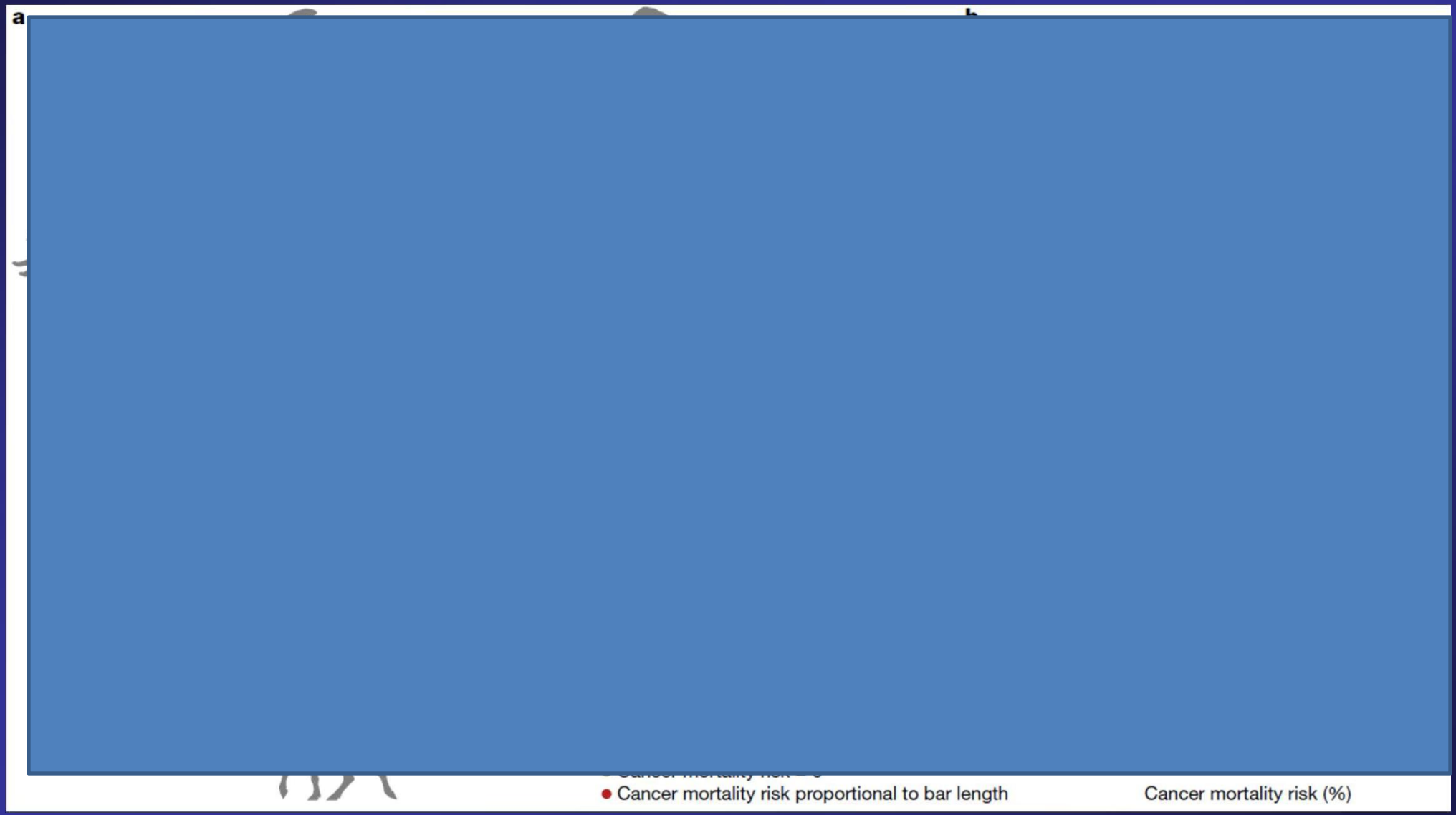
The Cell Cycle

p53



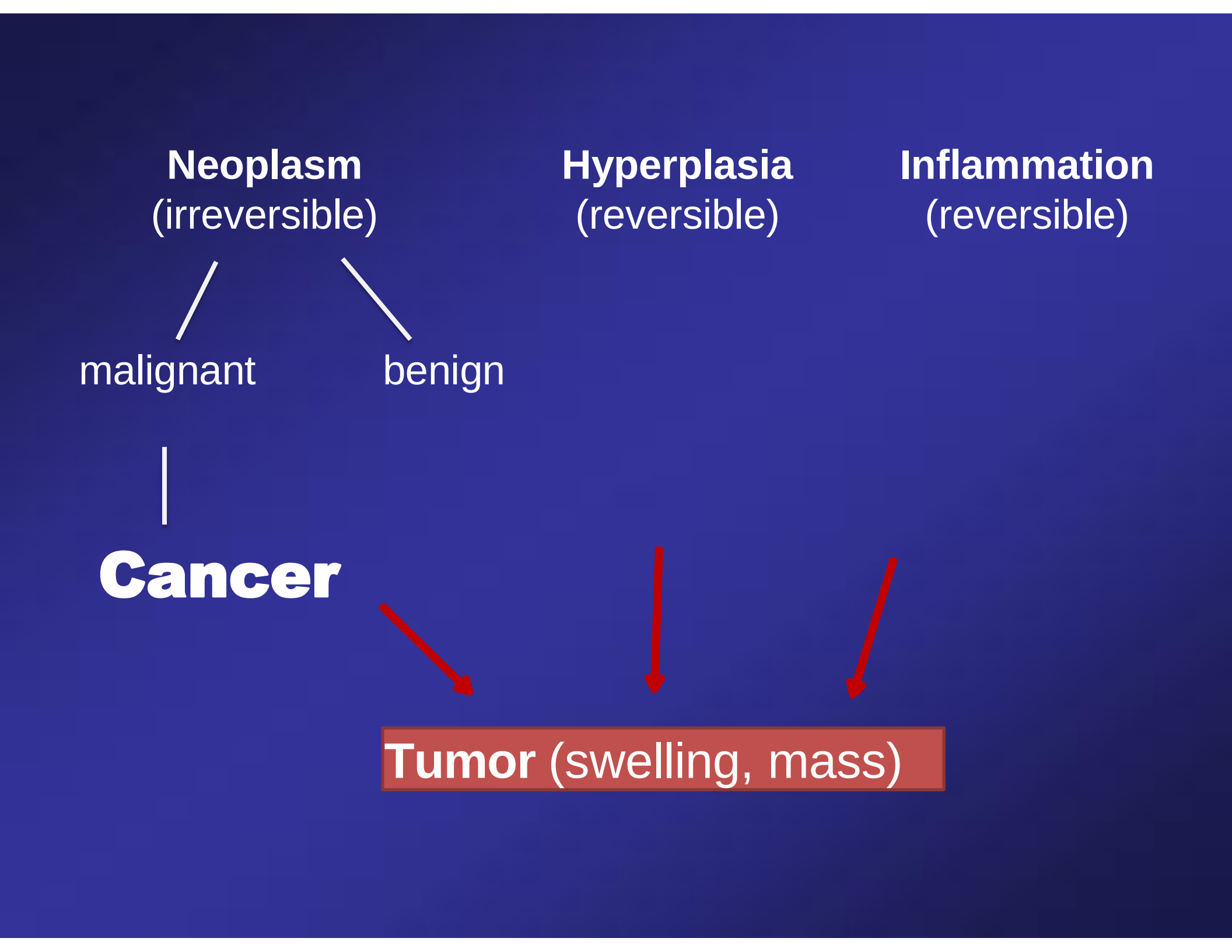
https://www.thermofisher.com/it/en/home/life-science/cell-analysis/cell-viability-and-regulation/cell-cycle.html

Distribution of cancer mortality risk across the mammalian phylogeny



Cancer mortality risk in mammals as a function of animal content in diet

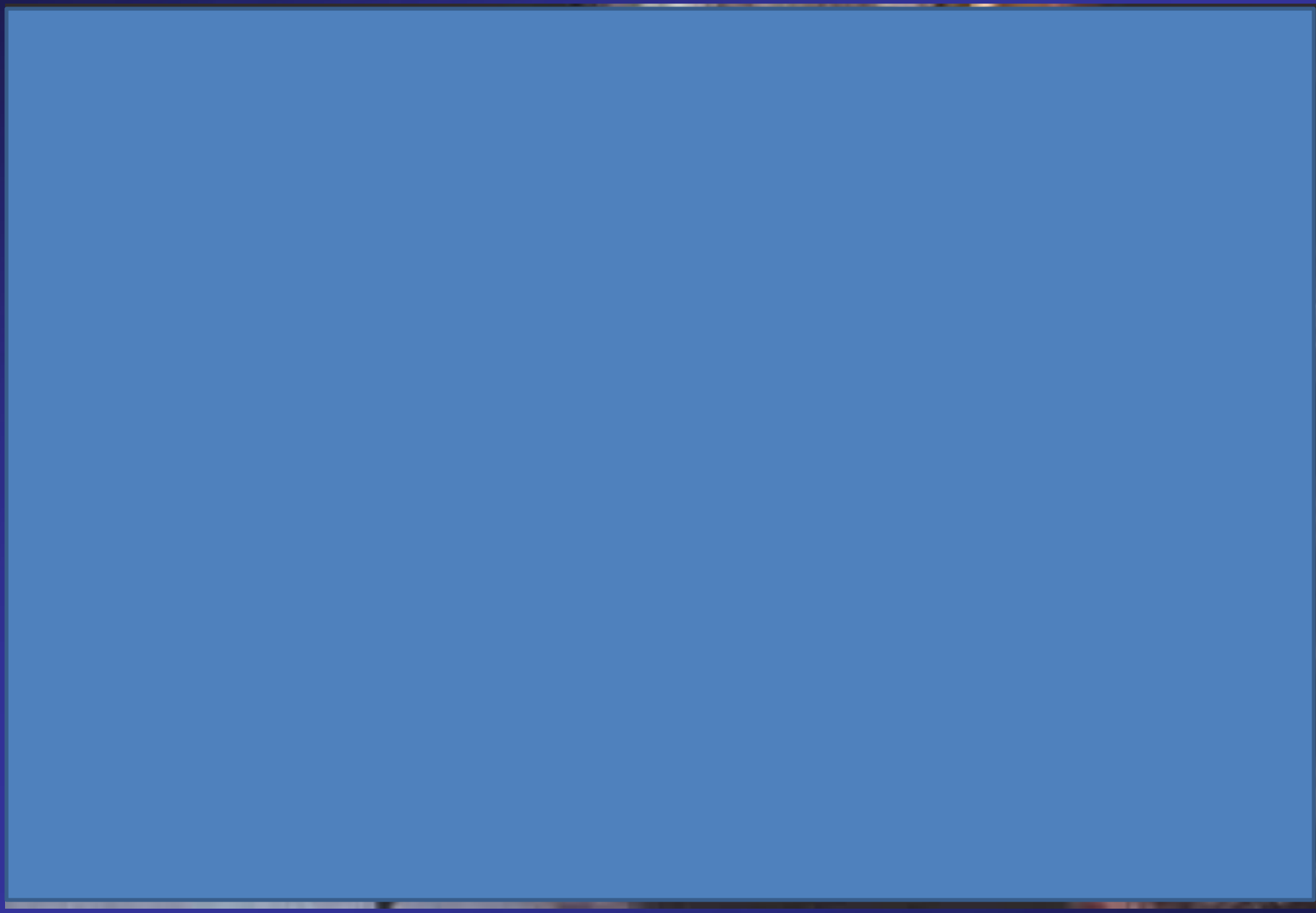
Nature | Vol 601 | 13 January 2022 |


Neoplasm
(irreversible)
Hyperplasia
(reversible)
Inflammation
(reversible)
malignant
benign
Cancer
Tumor (swelling, mass)

Inflammation: Granulation tissue

Mammary Gland: Fibroadenomatous Hyperplasia

Cutaneous Papillomas

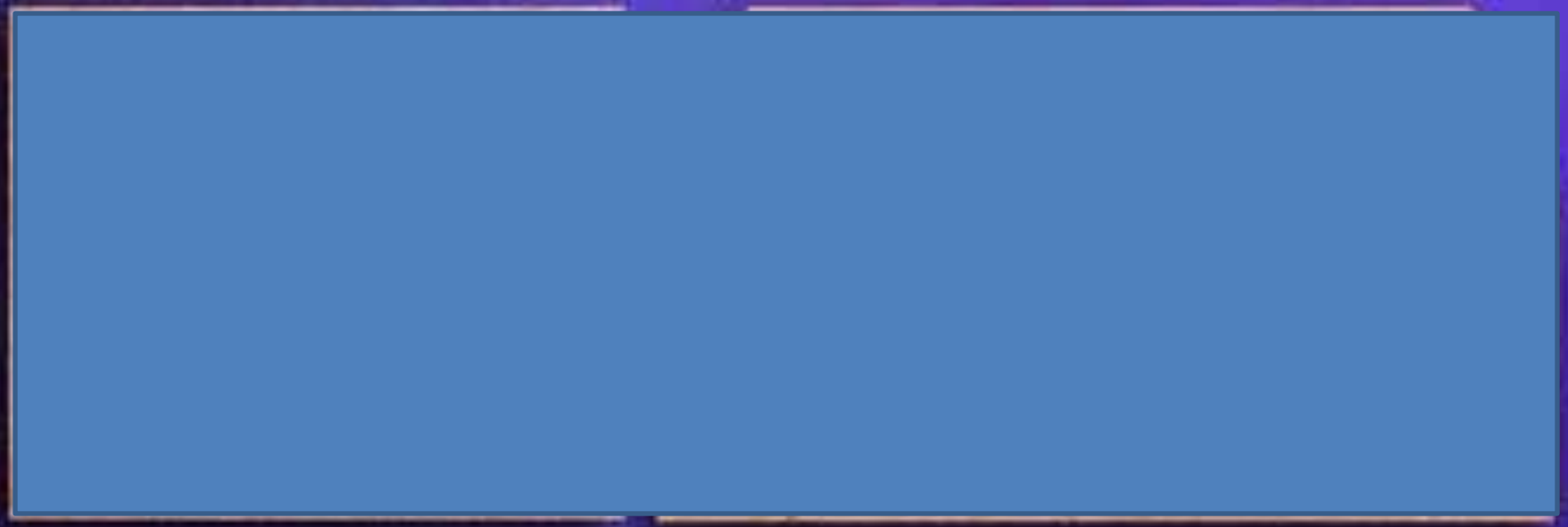


Melanoma

Melanoma

benign nevus malignant melanoma

Melanoma



benign nevus malignant melanoma

Nomenclature neoplasm

Tissue Type	Benign	Malignant
Epithelial	"-oma"	" - carcinoma"
Glandular	Adenoma (eg. Tubular adenoma of colon)	Adenocarcinoma (eg. Colon adenocarcinoma)
Squamous	Squamous papilloma	Squamous cell carcinoma
Mesenchymal	"-oma"	"- sarcoma"
Bone (osteo-)	Osteoma	Osteosarcoma
Blood vessels **Lymph vessels**	Haemangioma; Lymphangioma	Angiosarcoma Lymphangiosarcoma
Smooth muscle	Leiomyoma	Leiomyosarcoma
Skeletal muscle	Rhabdomyoma	Rhabdomyosarcoma
Cartilage	Chondroma	Chondrosarcoma
Fat	Lipoma	Liposarcoma

Animation: How Tumors Grow

https://youtu.be/payuQYLeu1E

https://www.biointeractive.org/classroom-resources/how-tumors-grow

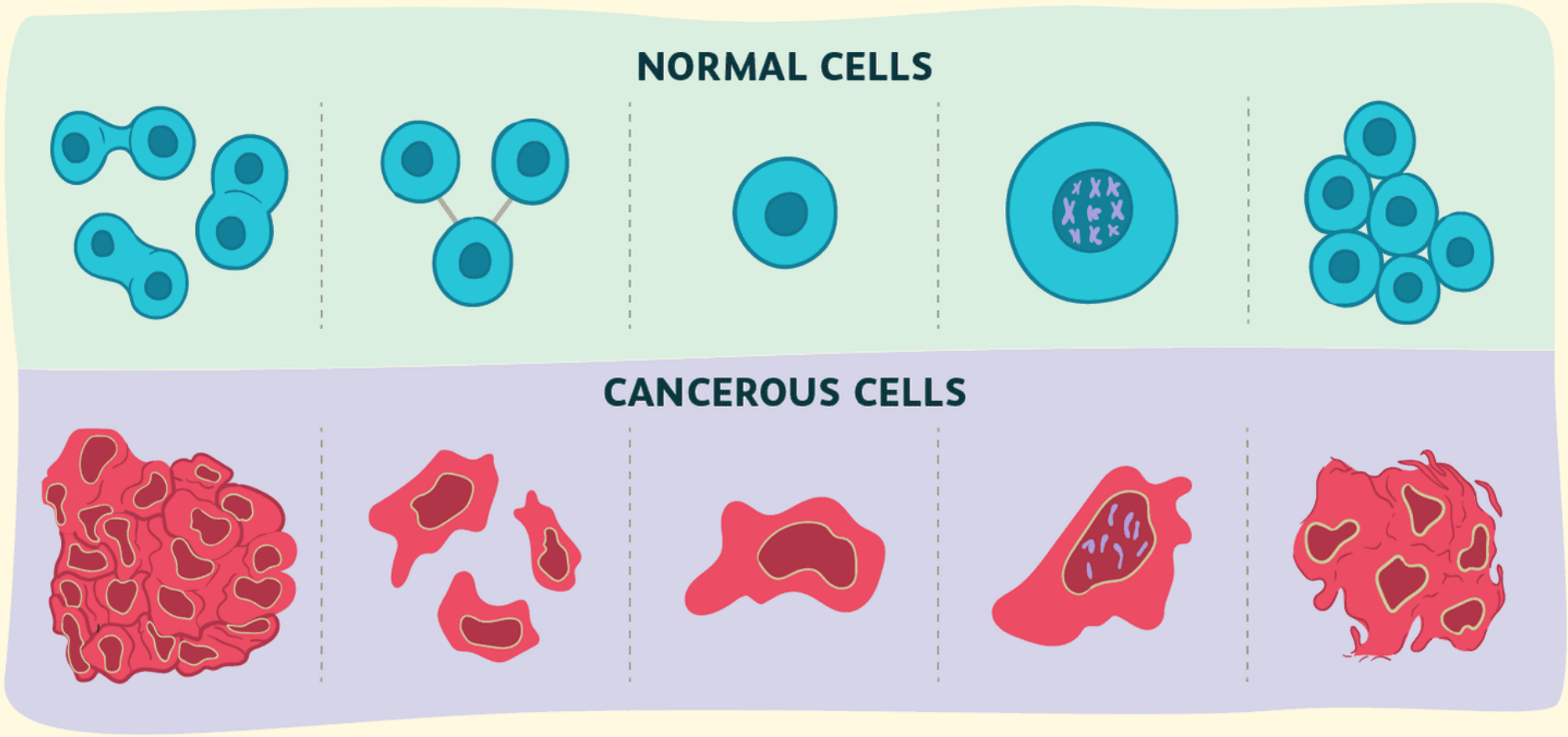
How to recognize cancer cells under the microscope?

Normal	Hyperplasia	Mild dysplasia	Carcinoma in situ (severe dysplasia)	Cancer (invasive)
	Hyperplasia	Dysplasia	Carcinoma Pre-invasivo	Carcinoma invasivo

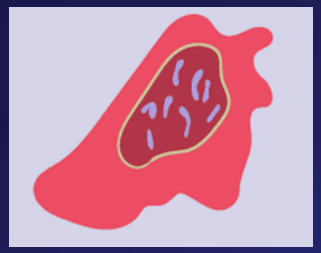
MAIN DIFFERENCES CANCER VS. NORMAL CELLS

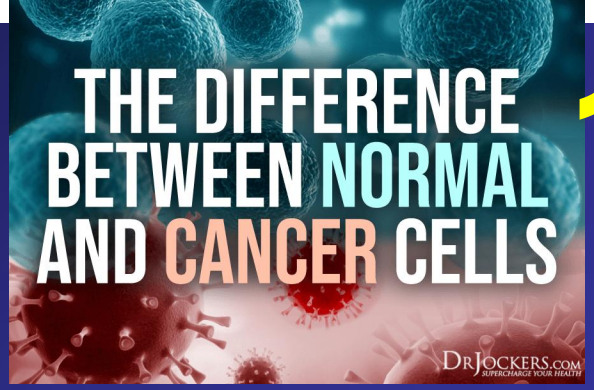
Normal cells	Cancer cells
Fine chromatin	Coarse chromatin
Single nucleus	Multiple nuclei
Single nucleolus	Multiple nucleoli
Large cytoplasm	Small cytoplasm

MAIN DIFFERENCES CANCER VS. NORMAL CELLS

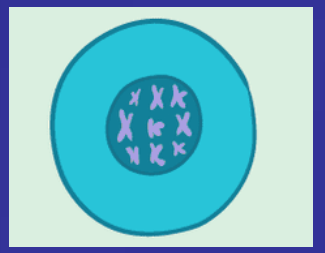


verywell





1



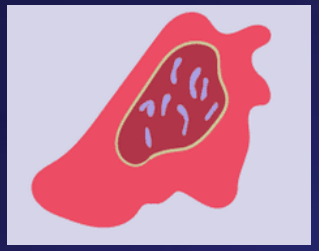
cancer cells:

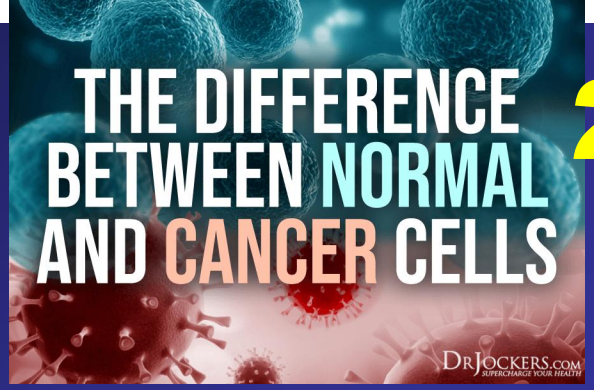
1. grow in the absence of signals telling them to grow.
2. ignore signals that normally tell cells to stop dividing or to die (a process known as programmed cell death, or apoptosis).
3. invade into nearby areas and spread to other areas of the body.
4. tell blood vessels to grow toward tumors. These blood vessels supply tumors with oxygen and nutrients and remove waste products from tumors.

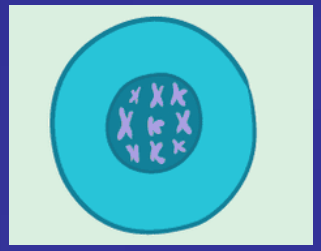
Normal cells

1. only grow when they receive such signals.
2. signals that normally tell cells to stop dividing or to die (a process known as programmed cell death, or apoptosis).
3. stop growing when they encounter other cells, and most normal cells do not move around the body.
4. They induce the production of new blood vessels always when needed by the body (wound healing)

https://www.cancer.gov/about-cancer/understanding/what-is-cancer#definition







cancer cells:

1. hide from the immune system.
2. trick the immune system into helping cancer cells stay alive and grow. For instance, some cancer cells convince immune cells to protect the tumor instead of attacking it.
3. accumulate multiple changes in their chromosomes
4. Different metabolism of the cells: make energy from nutrients in a different way than most normal cells. This lets cancer cells grow more quickly.

Normal cells

1. The immune system normally eliminates damaged or abnormal cells.
2. Immune cells attack all the “different” cells in the body
3. Normal number and structure of chromosomes
4. Normal metabolism to maintain homeastasis

https://www.cancer.gov/about-cancer/understanding/what-is-cancer#definition

Differences between Cancer Cells and Normal Cells/2

Many times, cancer cells rely so heavily on these **abnormal behaviors** that they can't survive without them.

Researchers have taken advantage of this fact,
developing therapies that target the abnormal features of cancer cells.

For example:
some cancer therapies prevent blood vessels from growing toward tumors, essentially starving the tumor of needed nutrients.

ADVANCED MATERIALS
www.advmat.de

Monotherapy and Combination Therapy Using Anti-Angiogenic Nanoagents to Fight Cancer

Pingping Liang, Byron Ballou, Xinyi Lv, Weili Si, Marcel P. Bruchez,* Wei Huang, and Xiaochen Dong**

Schematic representation of tumour growth.

La popolazione cellulare si espande
e una percentuale progressivamente sempre più alta di cellule tumorali lasciano il pool replicativo attraverso una reversione verso la fase G0, differenziazione e morte cellulare

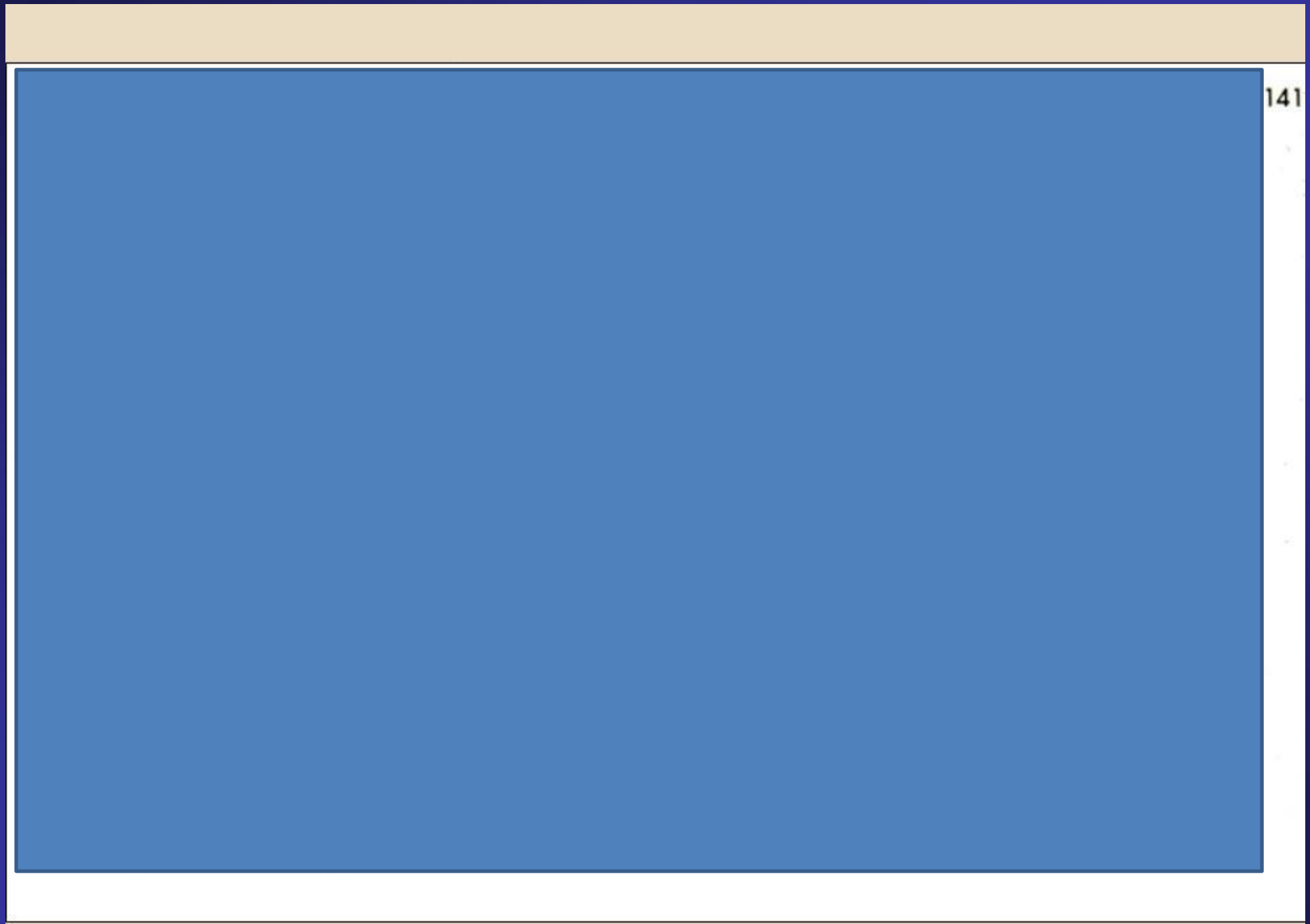
Robbins and Cotran_Pathologic Basis of Disease.

Comparison Benign and Malignant Tumors

	Benign	Malignant
Differentiation	**Well differentiated** **Structure similar to tissue of origin**	**Some lack of differentiation** **Structure often atypical**
Growth rate	Slow Rare mitotic figures	Rapid Numerous mitotic figures
Local Invasion*	Expansile growth Often capsule	Infiltrative growth No capsule
Metastasis*	No metastasis	Frequent metastasis

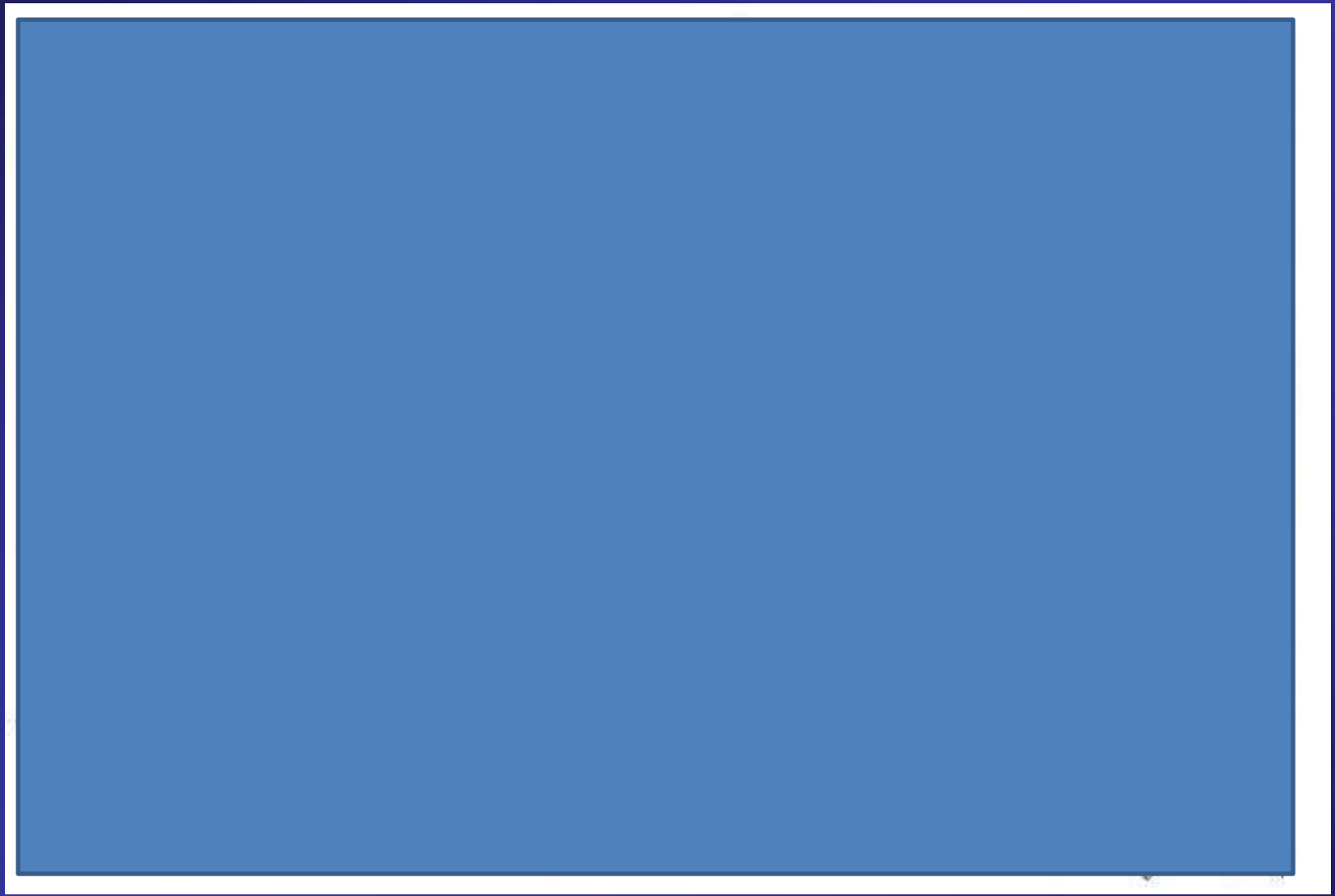
* Definitive criteria for malignancy

Example: Leiomyoma vs. Leiomyosarcoma



Robbins and Cotran_Pathologic Basis of Disease.

How do cancer cells invade through the basement membrane ?



Lysanne Hendrikx, 2010

Invasion of Basement Membrane by Cancer Cells

Loosening of
intercellular adhesion

Attachment

Lysanne Hendrikx, 2010

Invasion of Basement Membrane by Cancer Cells

Degradation

Migration

Lysanne Hendrikx, 2010

The metastatic cascade

Pathways of tumor metastasis

- Hematogenous
- Lymphatic
- Transcoelomic

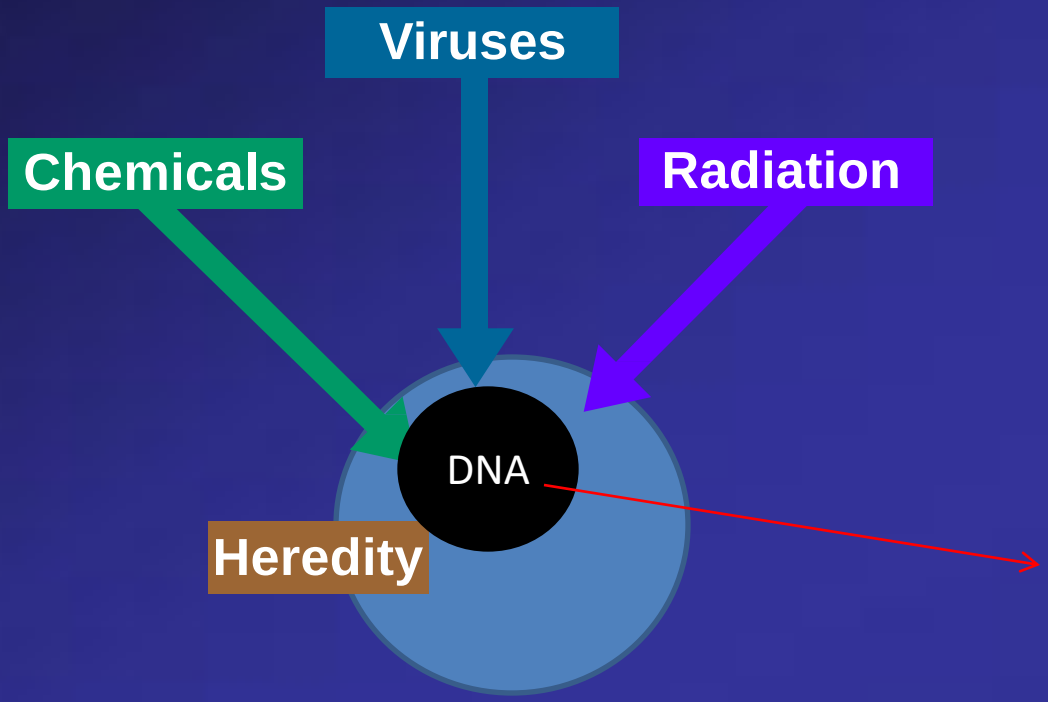
Hallmark of Cancer:
Activating Invasion and metastasis

Robbins and Cotran_Pathologic Basis of Disease.

In metastasis, cancer cells break away from where they first formed and form new tumors in other parts of the body.

https://www.cancer.gov/about-cancer/understanding/what-is-cancer#definition

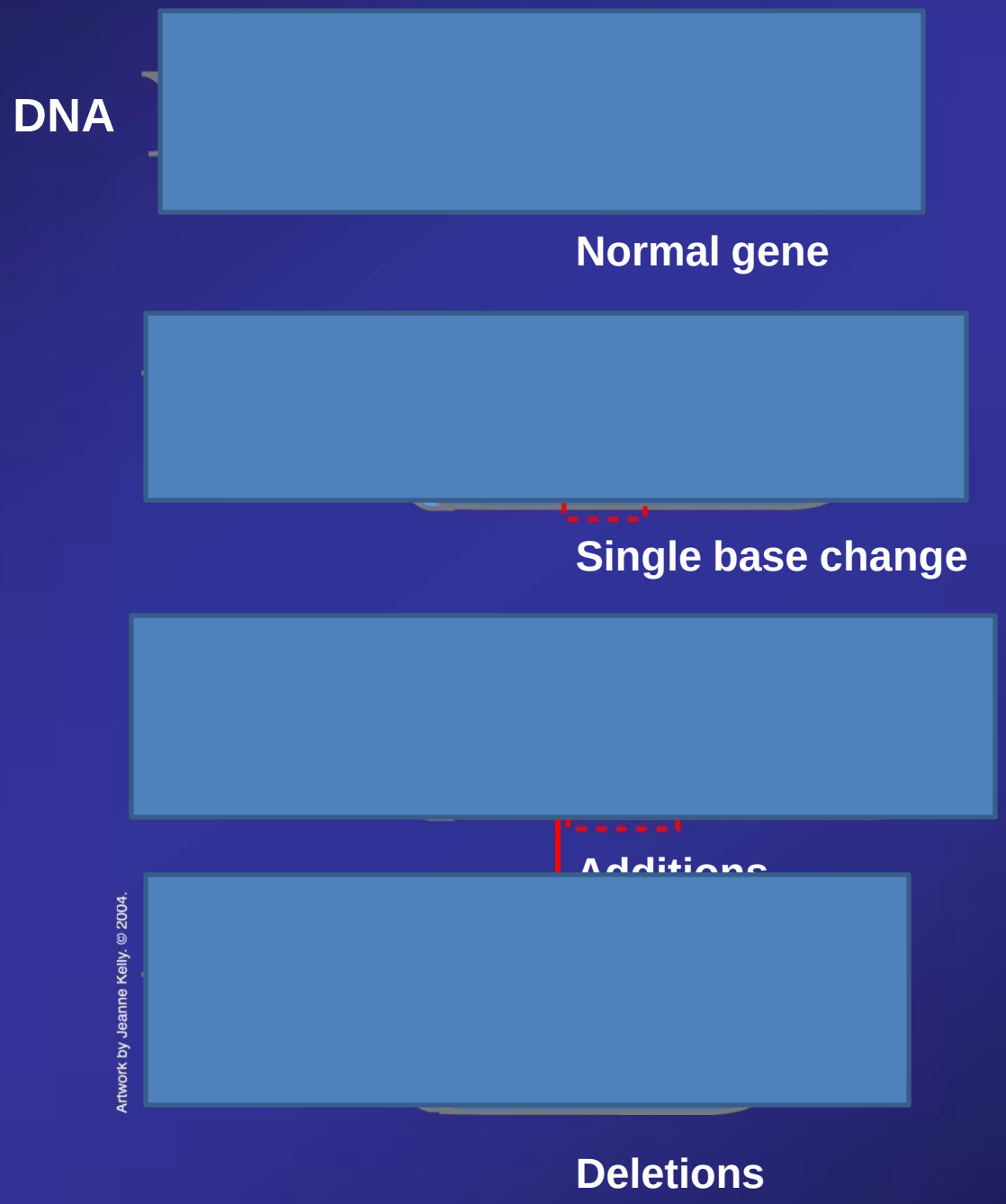
What Causes Cancer?



-> DNA Damage

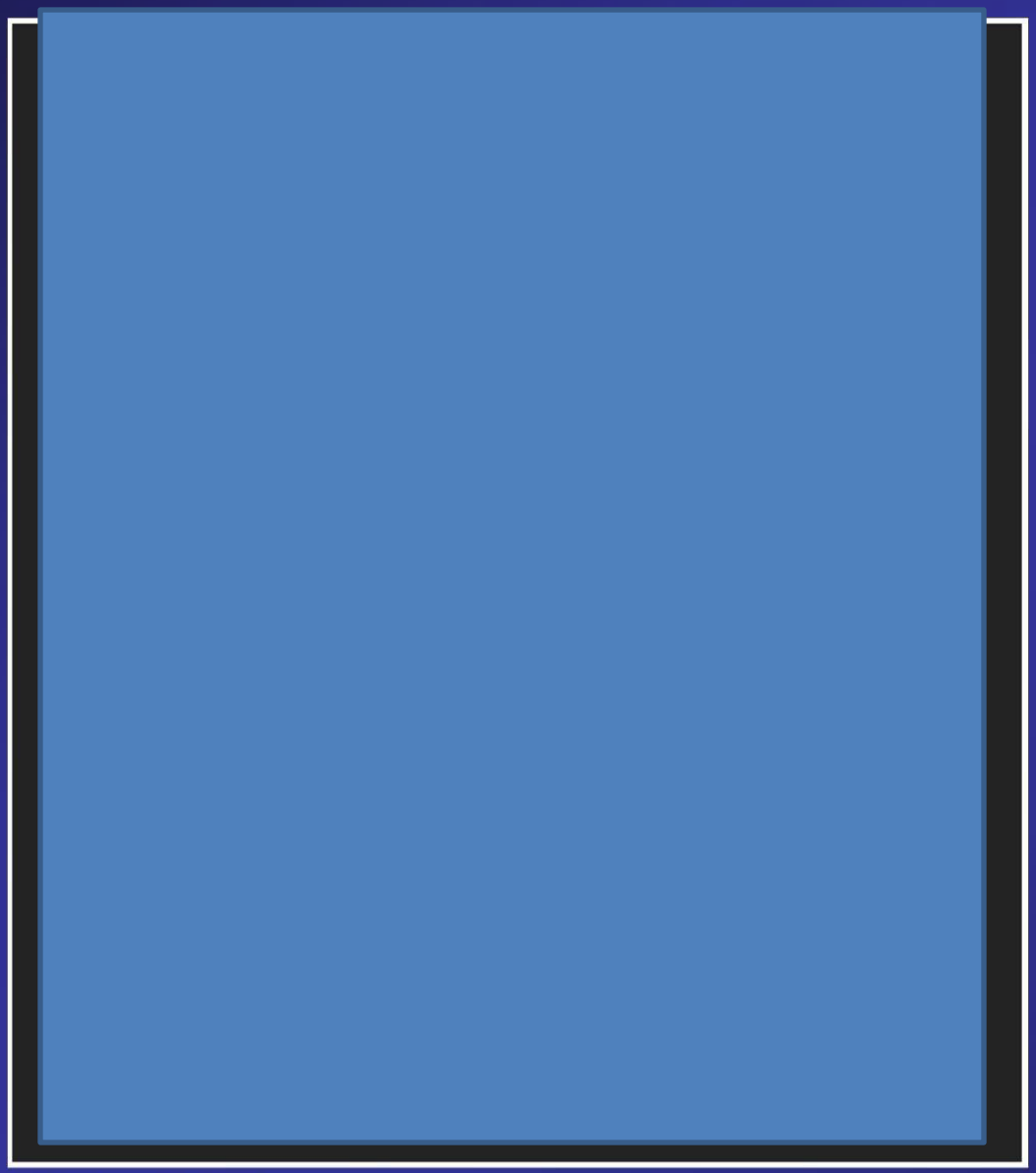
Chromosomes are DNA molecules

Genetic mutations



Chromosomal instability:

Aneuploidy, Translocation, Deletions, Amplification



Artwork by Jeanne Kelly. © 2004.

SKY chromosome painting: breast cancer

Hallmark of cancer:
Genomic instability

Normal SKY chromosomes are not multicolored.

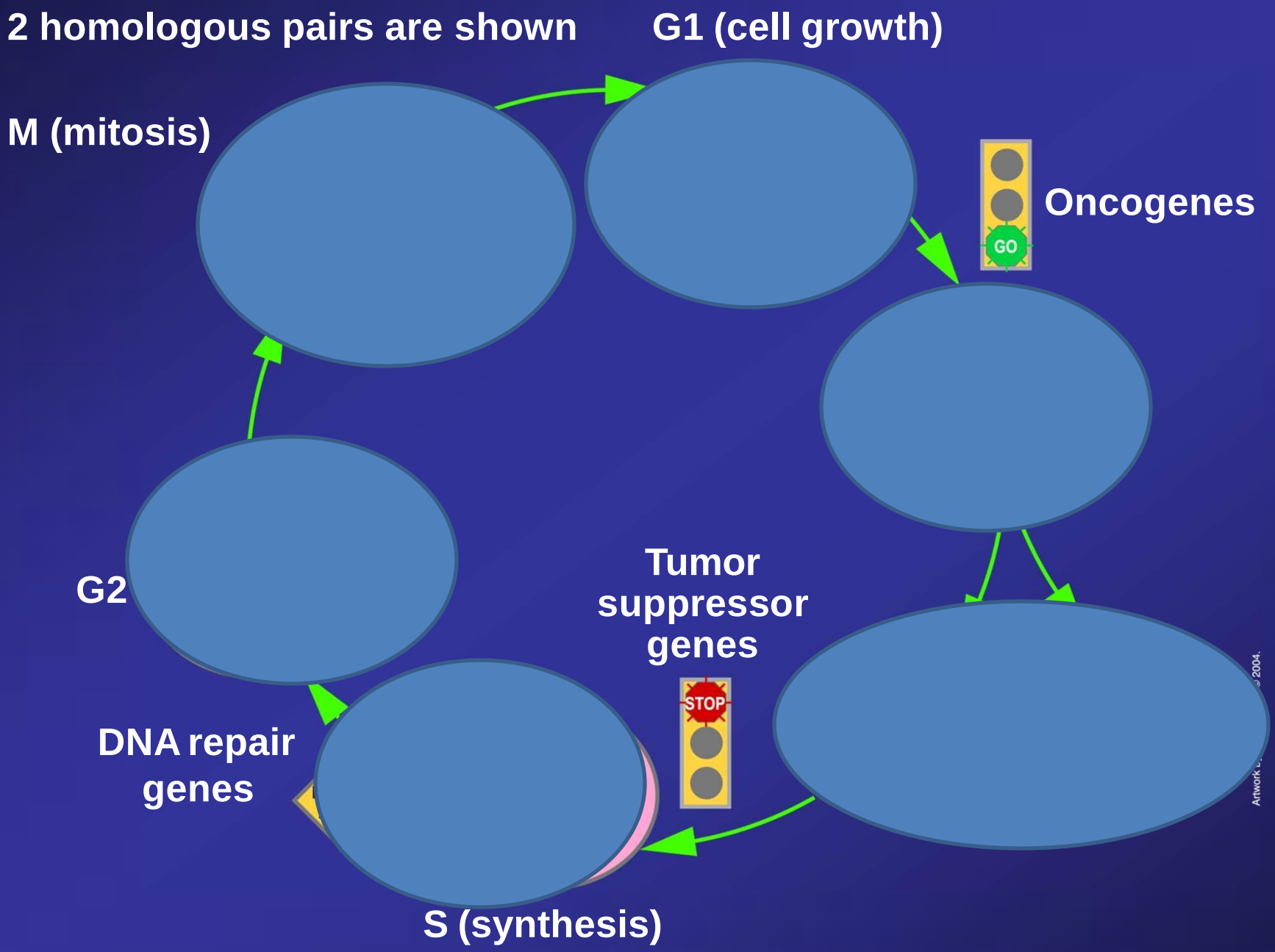
Chromosomes in breast cancer appear multicolored because they have exchanged genetic material.

Which genes are mutated in cancer ?

Genes Implicated in Cancer

The prime suspects	*But*
Mutations in:	Other mutations also occur in:
■ Oncogenes	■ Cell death genes
■ Tumor suppressor 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 Cell Growth: The Cell Cycle



Abnormal Cell Growth: Oncogenes

Oncogene: Ras

Robbins and Cotran_Pathologic Basis of Disease.

Hallmark of cancer:

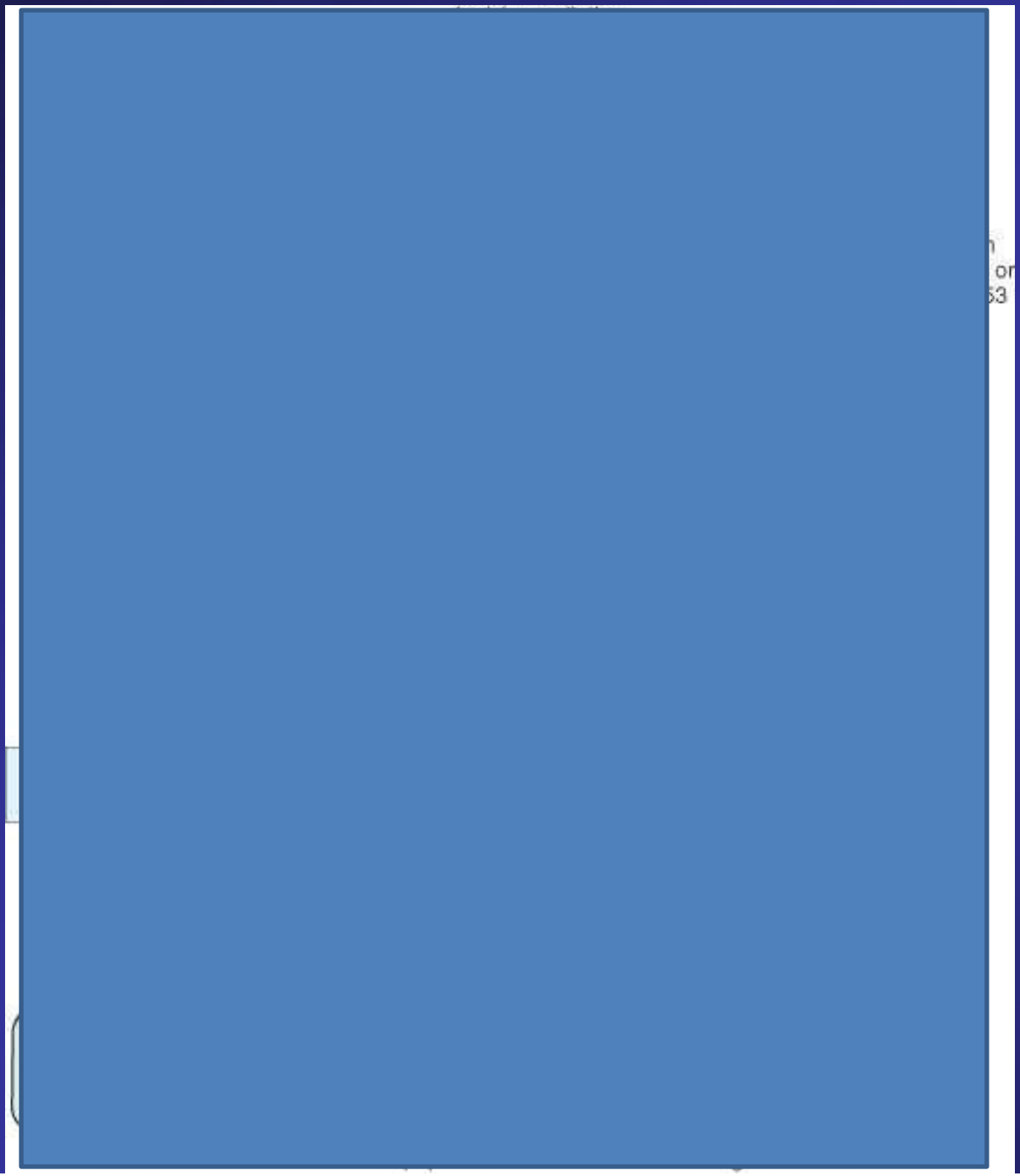
Sustaining proliferative signaling

Tumor Suppressor Genes

Active oncogene

Mutations in Tumor Suppressor Genes

Tumor Suppressor: p53



Hallmark of Cancer:
Evading
growth suppressors

Hallmark of Cancer:
Resisting
cell death

Robbins and Cotran_Pathologic Basis of Disease.

Mutations in Cancer Genes Are Sometimes Inherited …

….but most develop after birth

Examples of Dominantly Inherited Cancer Syndromes

Syndrome	Associated Gene
Familial retinoblastoma	*RB1*
Li-Fraumeni	*TP53* (p53 protein)
Familial adenomatous polyposis	*APC*
Hereditary nonpolyposis colorectal cancer	*MLH1, MSH2, MSH6 PMS1, PMS2*
Wilms' tumor	*WT1*
Breast and ovarian cancer	*BRCA1, BRCA2*
von Hippel-Lindau	*VHL*
Cowden	*PTEN*

Cancer Stem Cells

Reya et al. Nature (2001) 414: 105-111

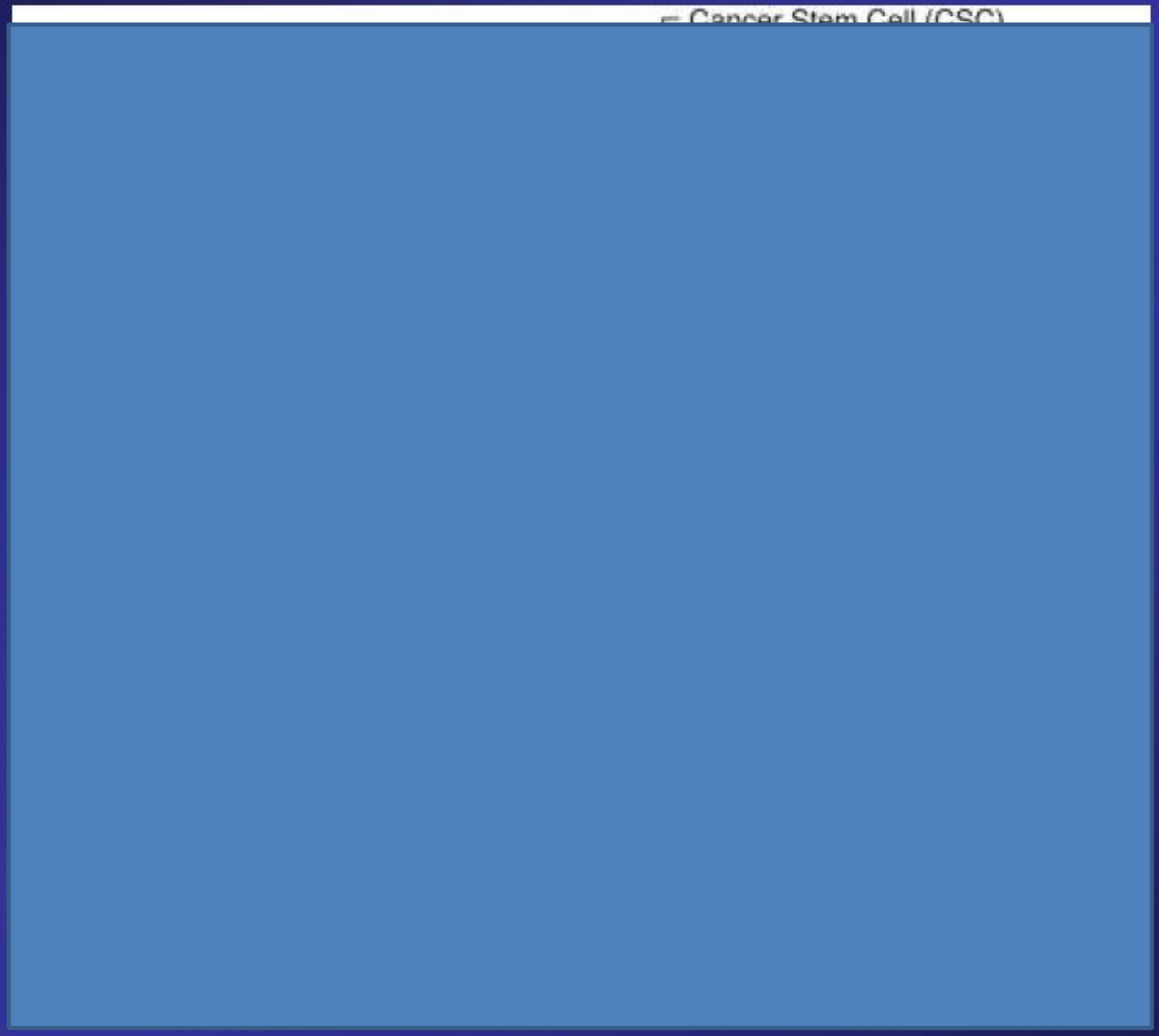
The Hallmarks of Cancer

Cell 144, March 4, 2011

Emerging Hallmarks of Cancer

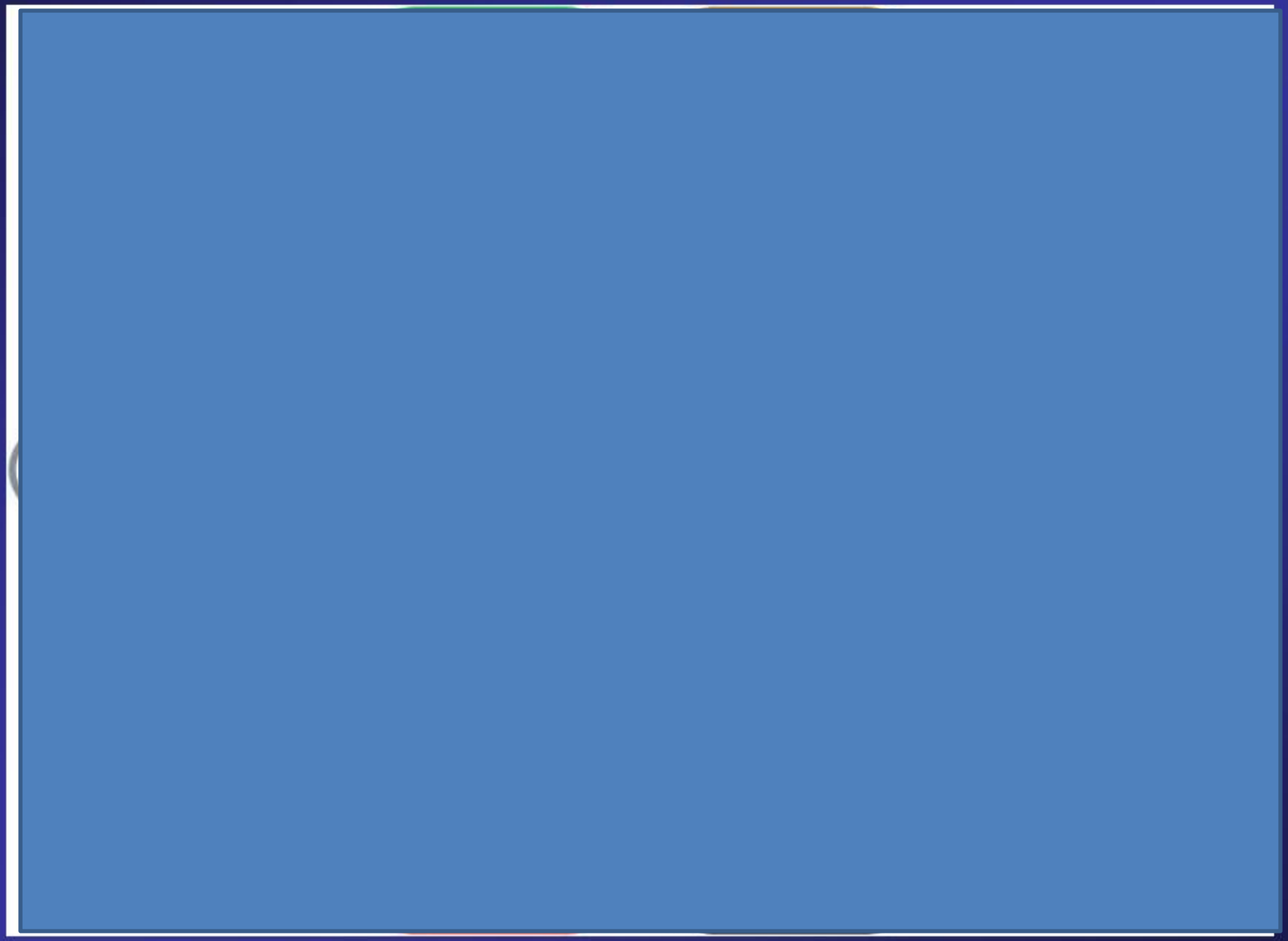
Cell 144. March 4. 2011

The cells of tumor microenvironment



Cell 144, March 4, 2011

Therapeutic targeting the hallmarks of cancer



Cell 144, March 4, 2011