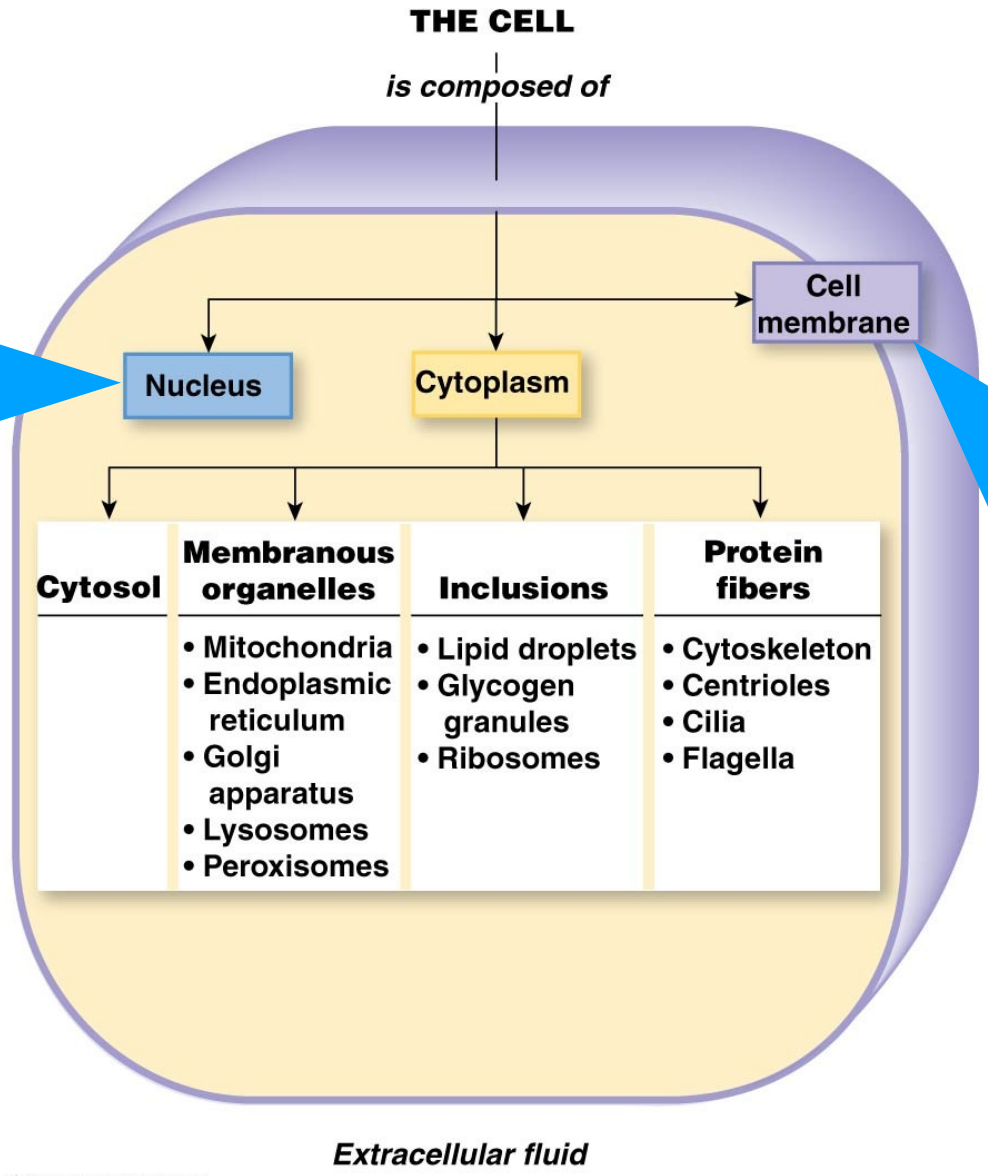

The Life and Death
of Cells

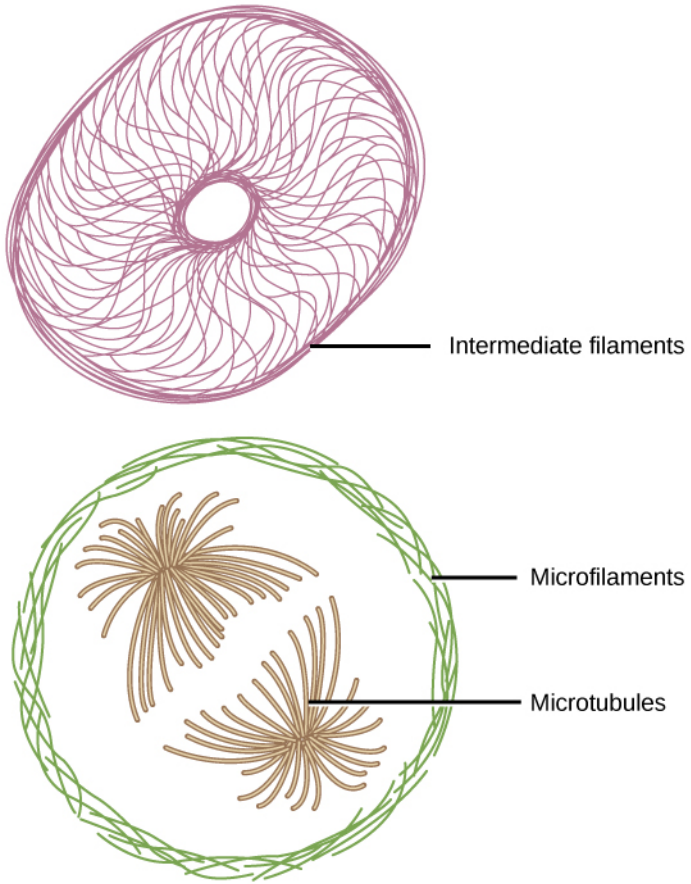
next time!

later

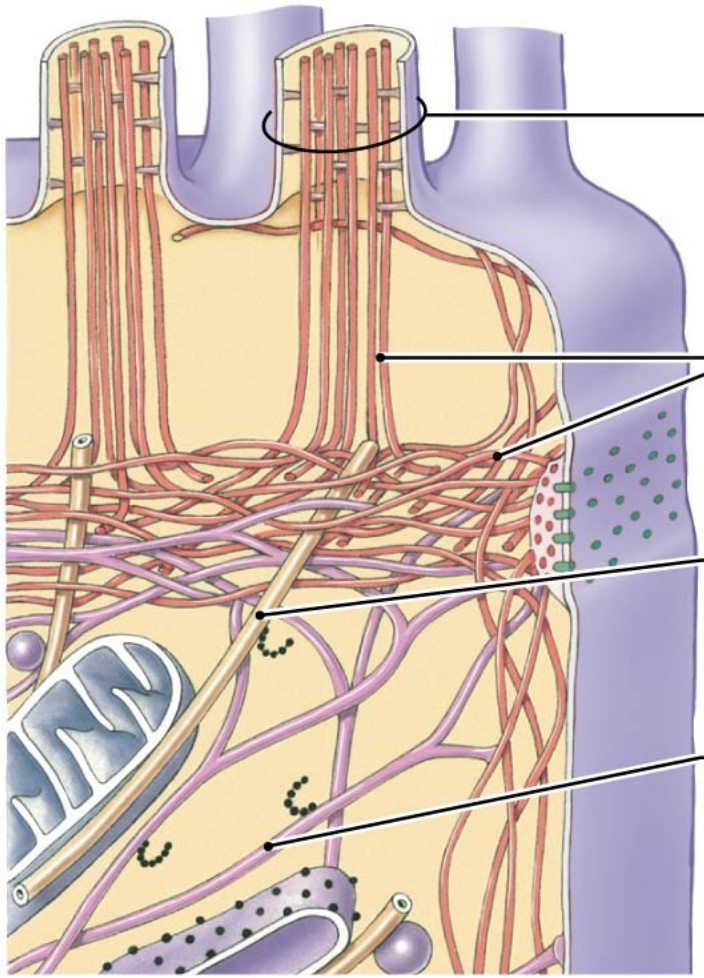


The Cytoplasm and Cytoskeleton

- Cytoplasm = interior soup of the cell
- Cytoskeleton provides structural support



(b) Cytoskeleton

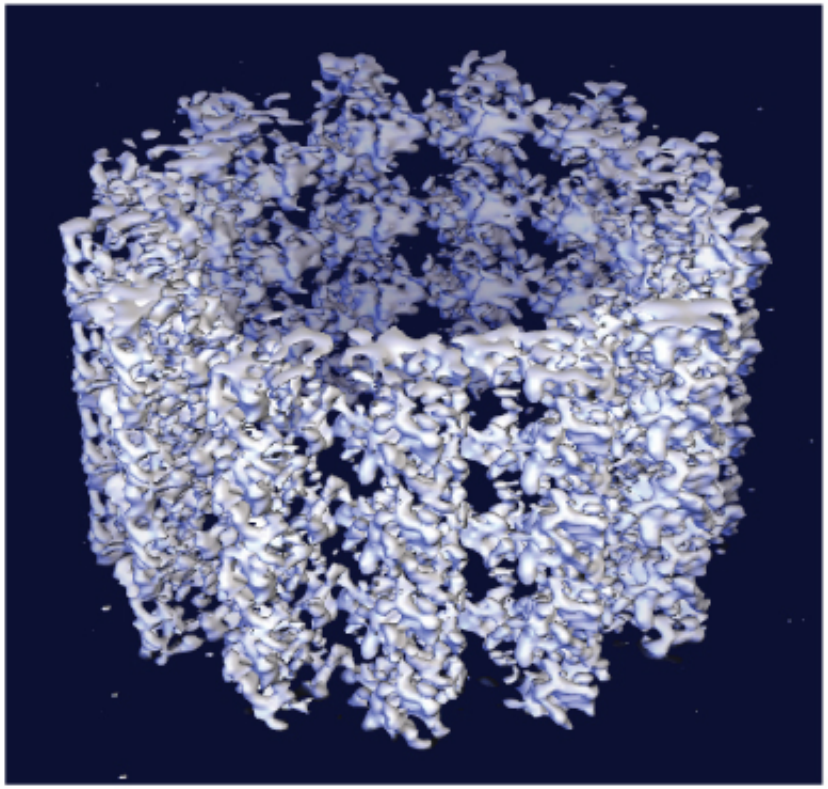


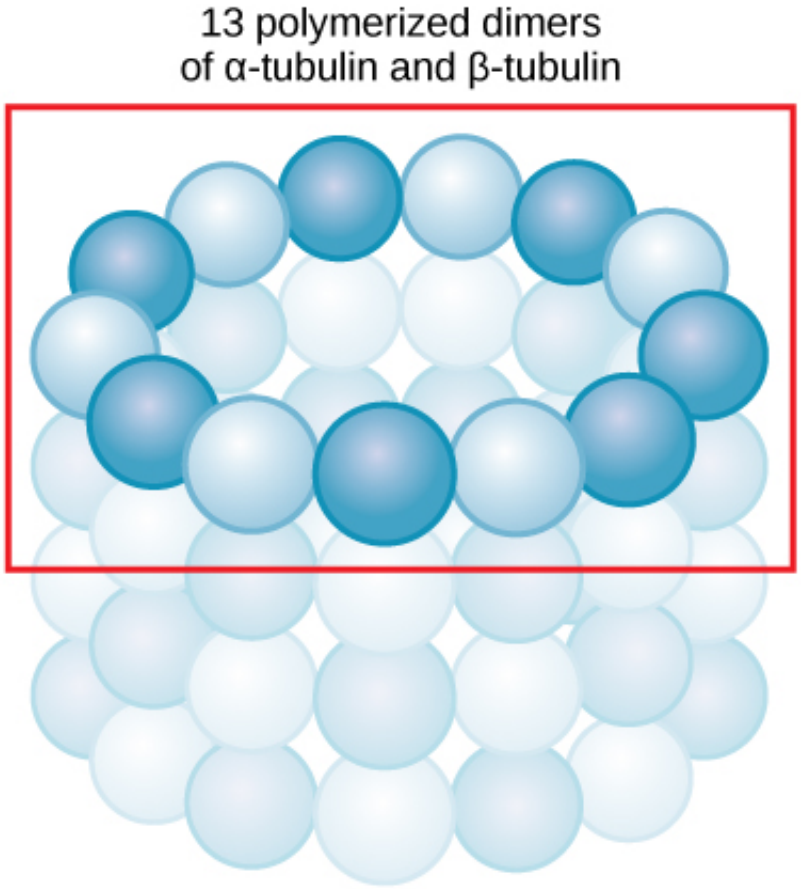
Microvilli increase cell surface area. They are supported by microfilaments.

Microfilaments form a network just inside the cell membrane.

Microtubules are the largest cytoskeleton fiber.

Intermediate filaments include myosin and keratin.

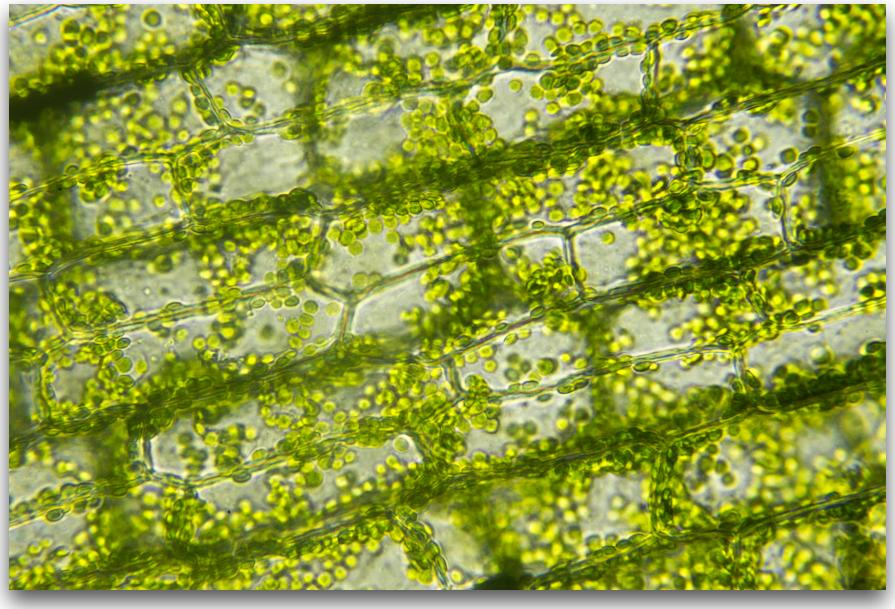




Microtubules are hollow. Their walls consist of 13 polymerized dimers of α-tubulin and β-tubulin (right image). The left image shows the tube's molecular structure.

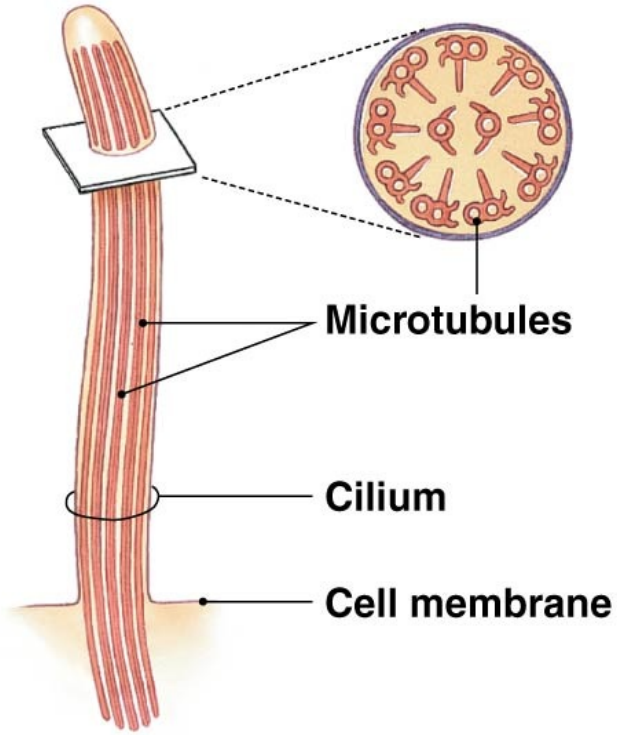
Cytoskeleton

- Movement, growth, organelle streaming, cell shape maintenance and repair requires this structural framework
- And some specialities...

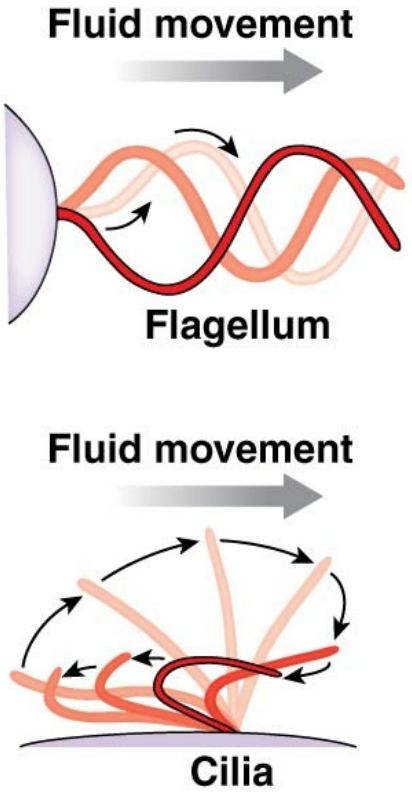


Chloroplasts stream around on cytoskeletal “freeways” in *Elodea*

(a) Cilia



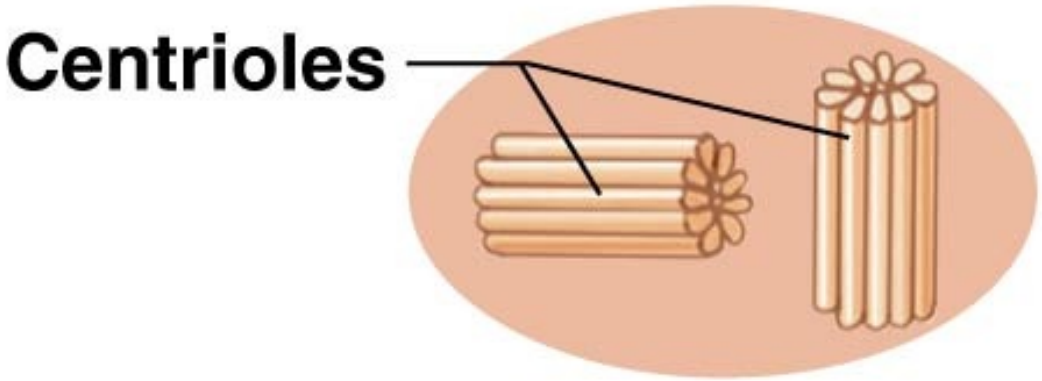
(b) Cilia and flagella have 9 pairs of microtubules surrounding a central pair.



(c) The beating of cilia and flagella creates fluid movement.

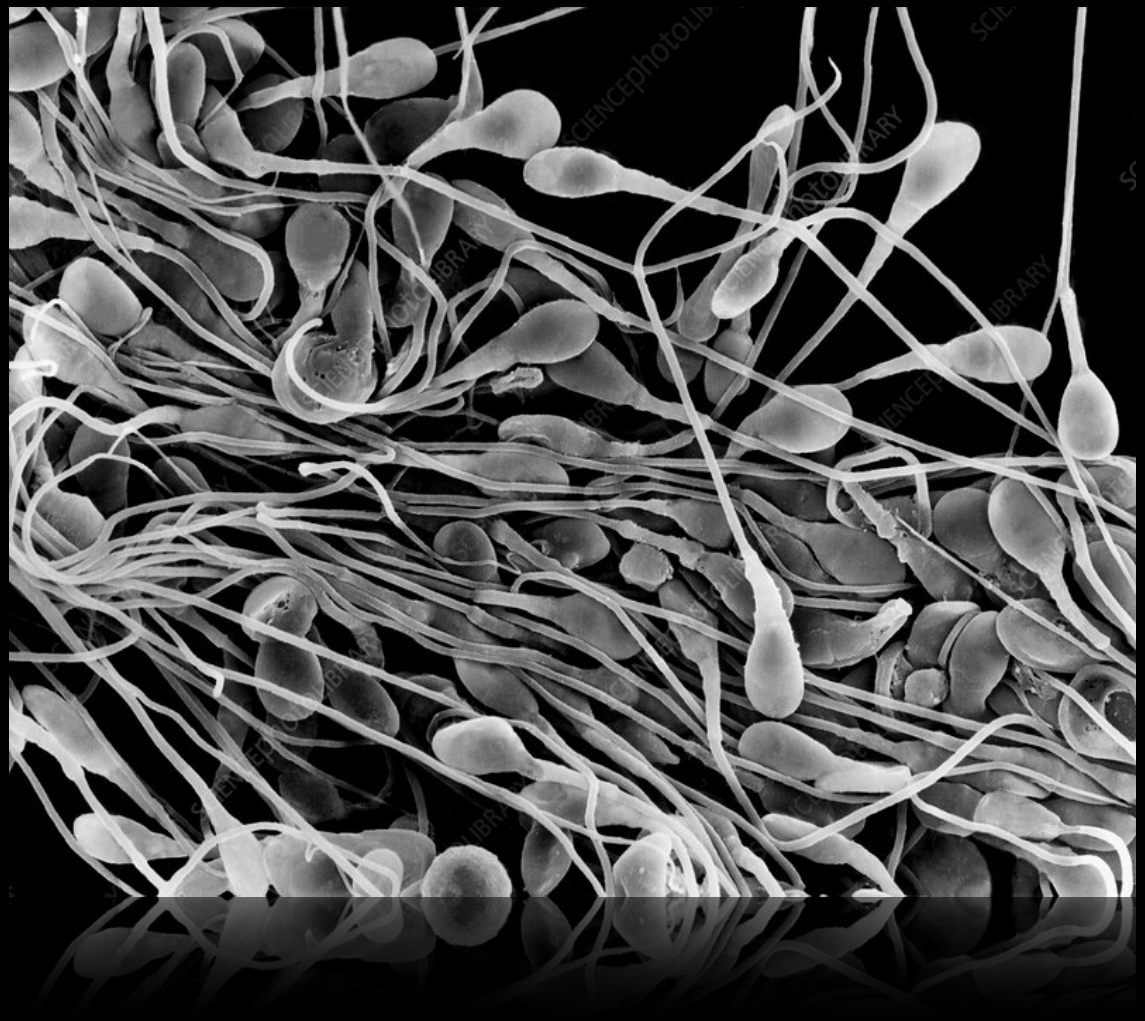
(e) Centrioles

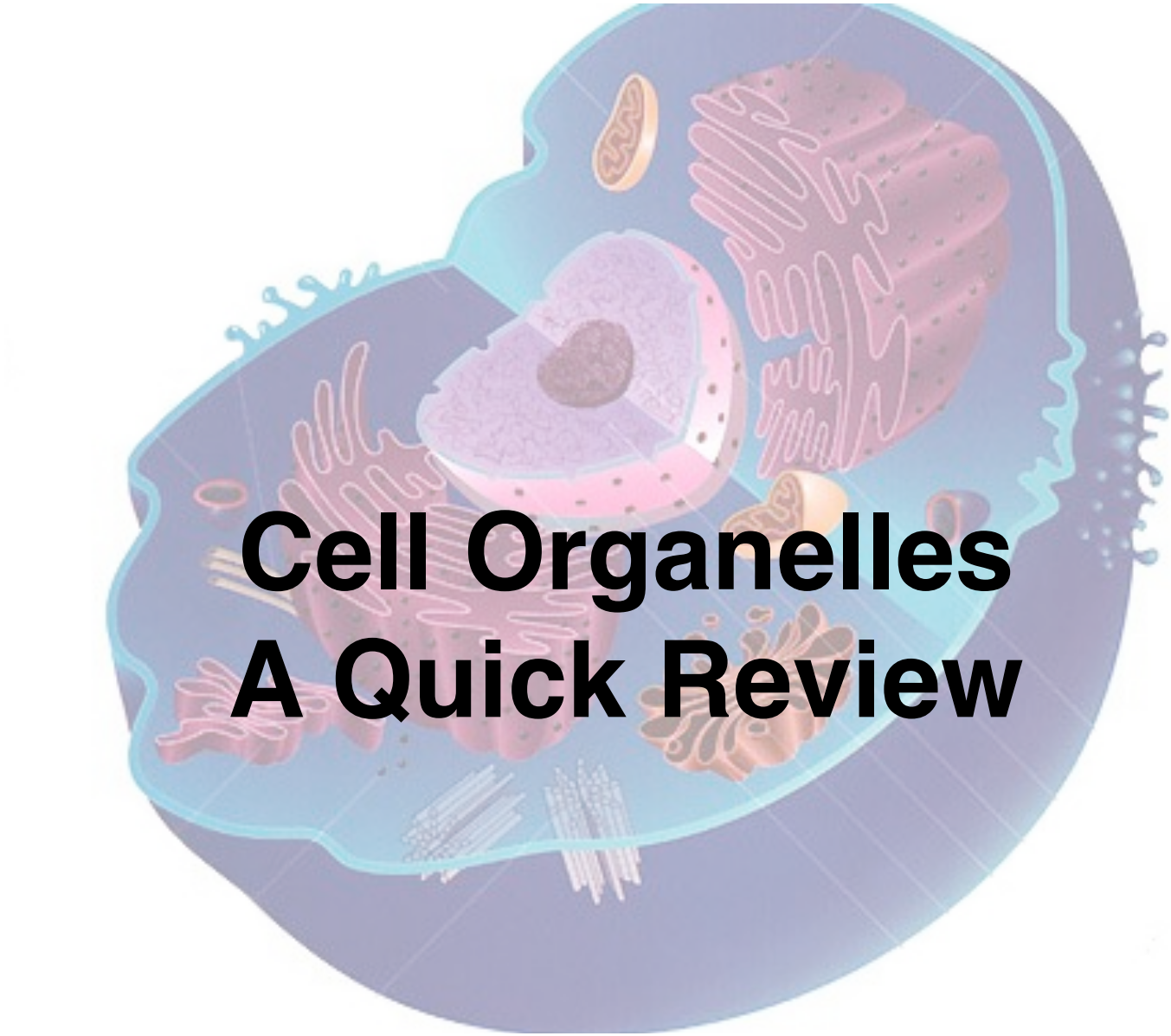
Centrioles are made from microtubules and direct DNA movement during cell division.



Human sperm cells visualized with SEM

Each sperm cell is 50 μm long and the head is 5 μm long



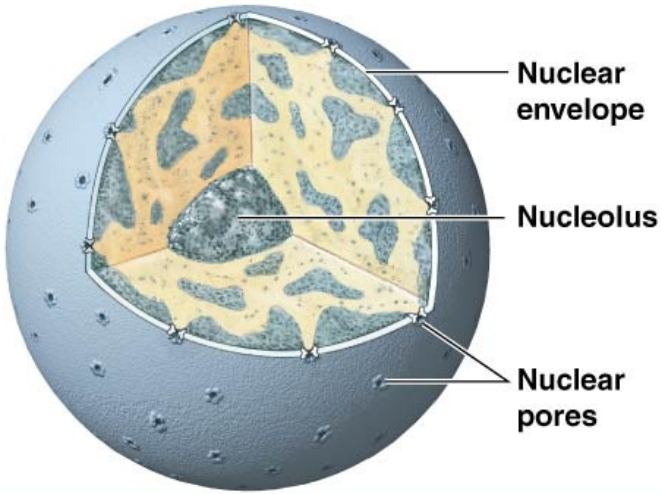


Cell Organelles
A Quick Review

Nucleus

- Control center
- Contains DNA
  - What does that DNA do?
  - Which parts of the DNA are read?
  - What happens when DNA is damaged?

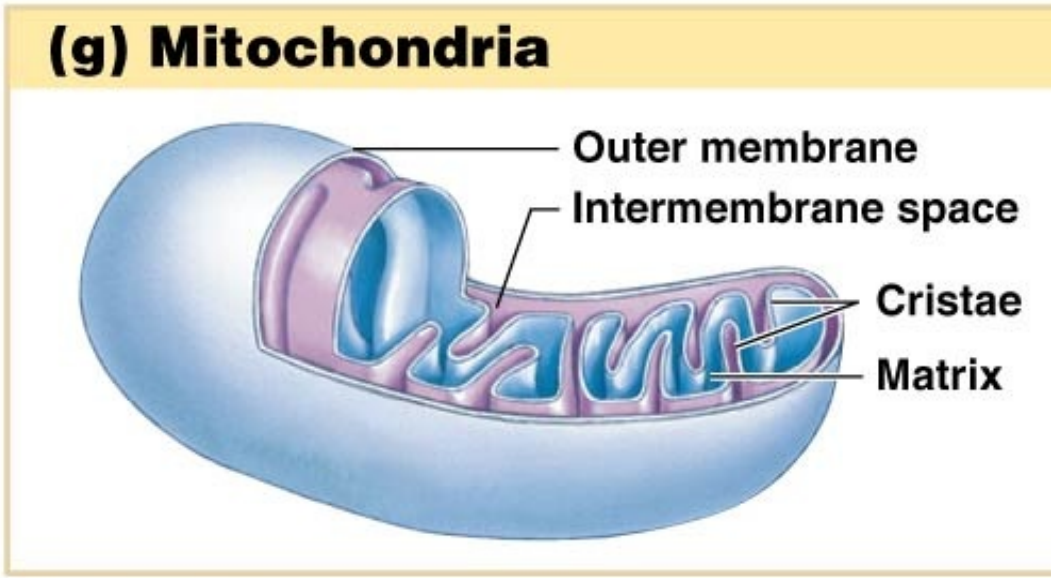
(j) Nucleus

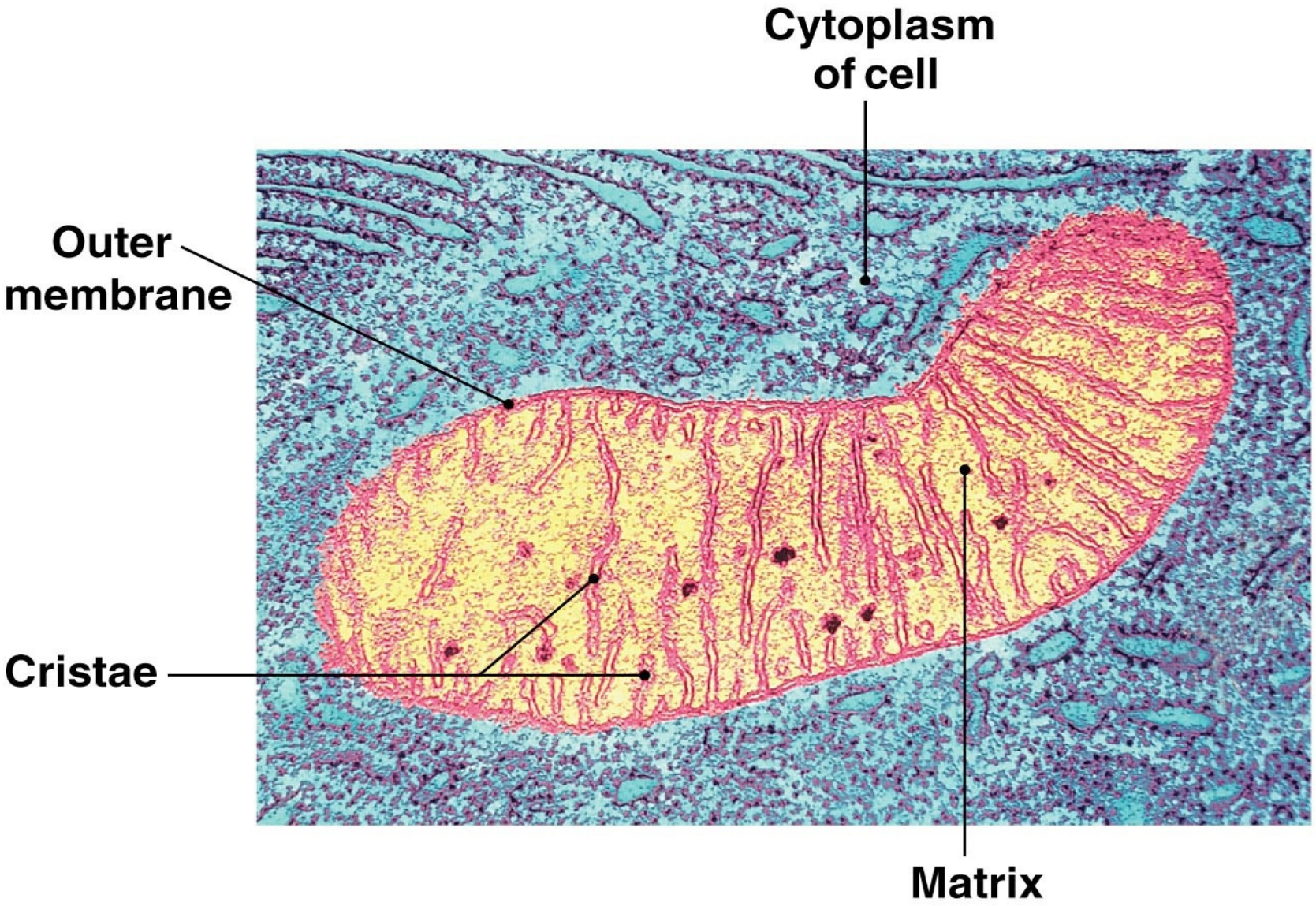


The **nucleus** is surrounded by a double-membrane **nuclear envelope**. Both membranes of the envelope are pierced here and there by **pores** to allow communication with the cytoplasm. The outer membrane of the nuclear envelope connects to the endoplasmic reticulum membrane. In cells that are not dividing, the nucleus appears filled with randomly scattered granular material composed of DNA and proteins. Usually a nucleus also contains from one to four larger dark-staining bodies of DNA, RNA, and protein called **nucleoli**.

Mitochondria

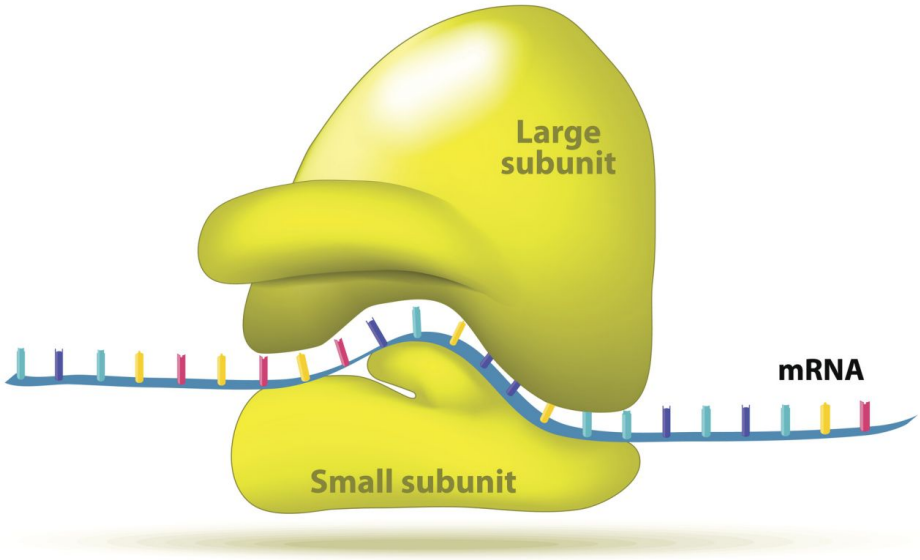
- Aerobic respiration
  - what goes in?
  - what comes out?
  - how is energy transformed?
- Contains DNA of its own
  - What?

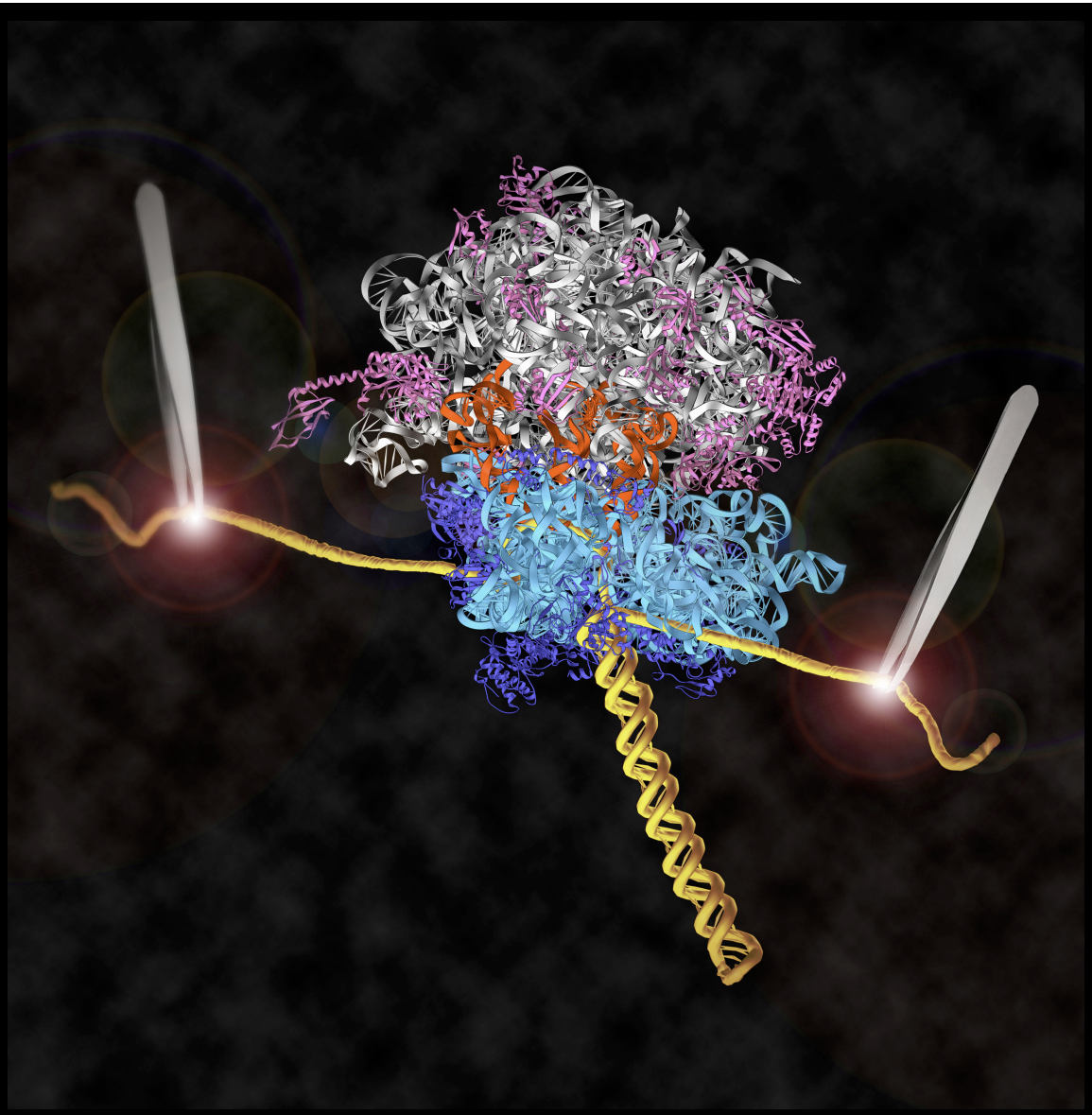



Cytoplasm of cell
Outer membrane
Cristae
Matrix

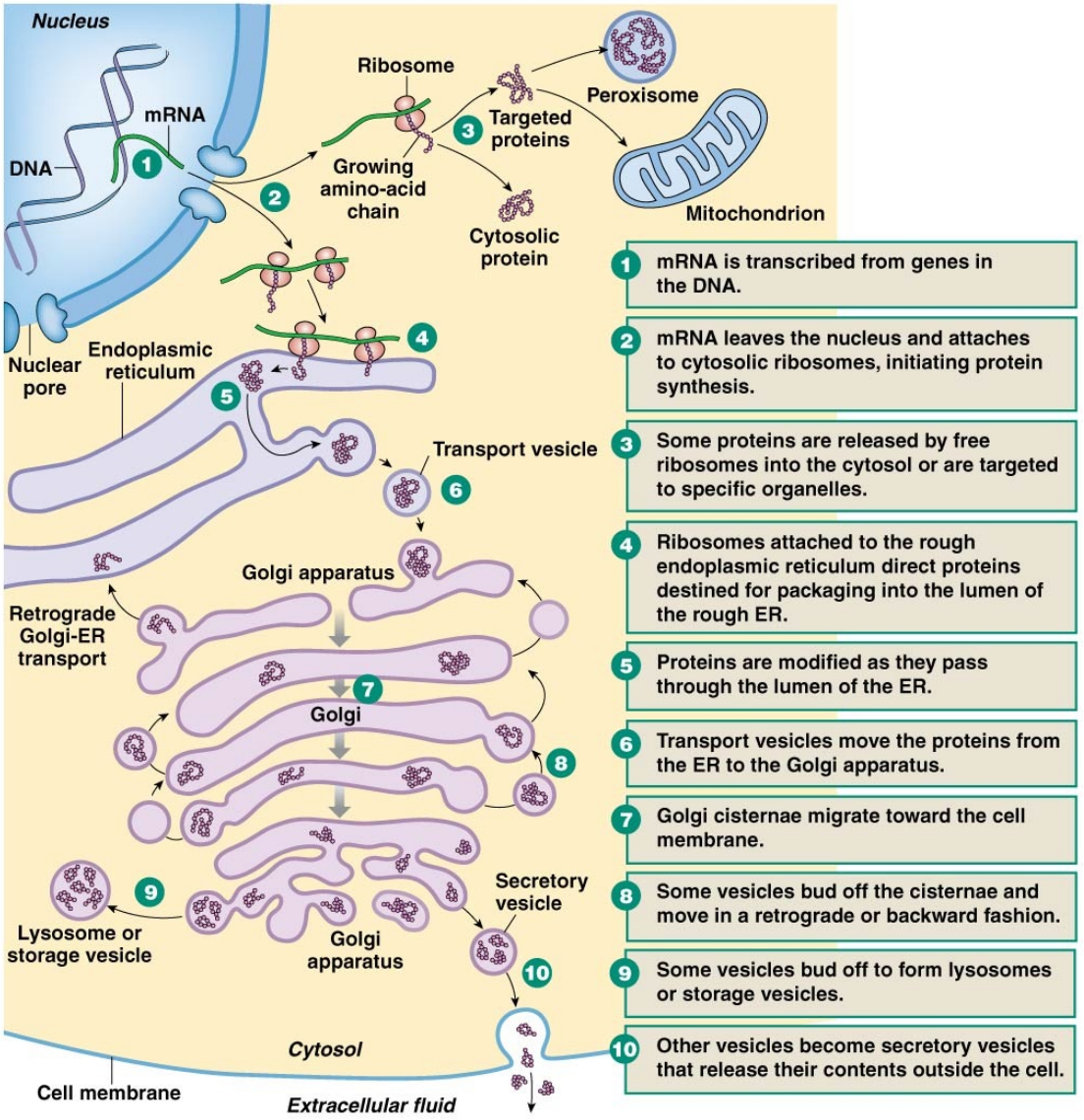
Ribosomes

- Site of protein synthesis
- 2 subunits, made of RNA and protein
- Float free or attached to rough ER





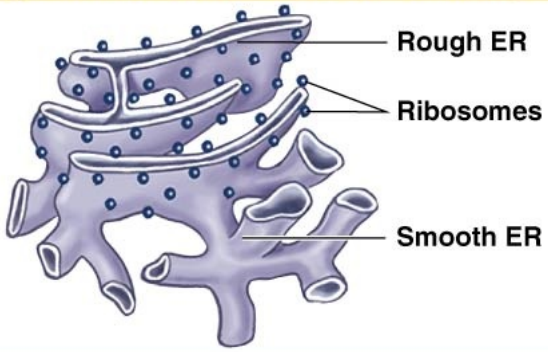
Endomembrane System



Endoplasmic Reticulum

- Rough ER
  - Makes membranes and proteins for export out of the cell or to be embedded in the membrane

(i) Endoplasmic Reticulum (ER)

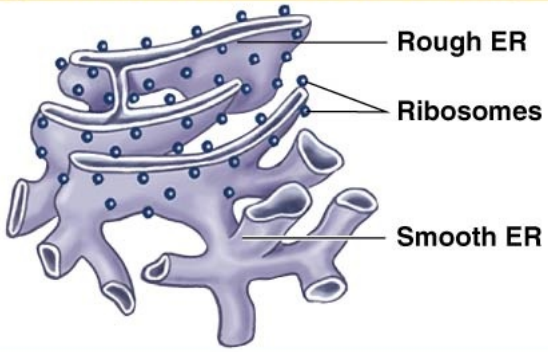


The **endoplasmic reticulum (ER)** is a network of interconnected membrane tubes that are a continuation of the outer nuclear membrane. **Rough endoplasmic reticulum** has a granular appearance due to rows of ribosomes dotting its cytoplasmic surface.

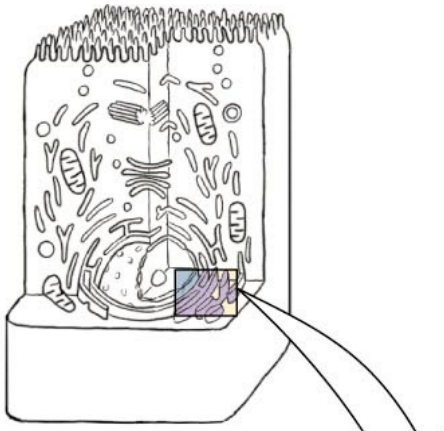
Endoplasmic Reticulum

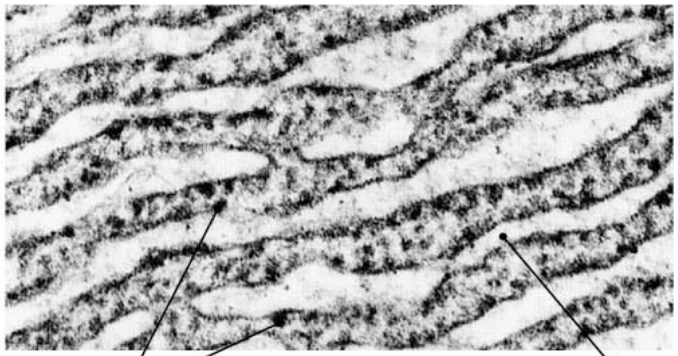
- Smooth ER
  - Synthesis of lipids
  - Stores Ca^{++}

(i) Endoplasmic Reticulum (ER)



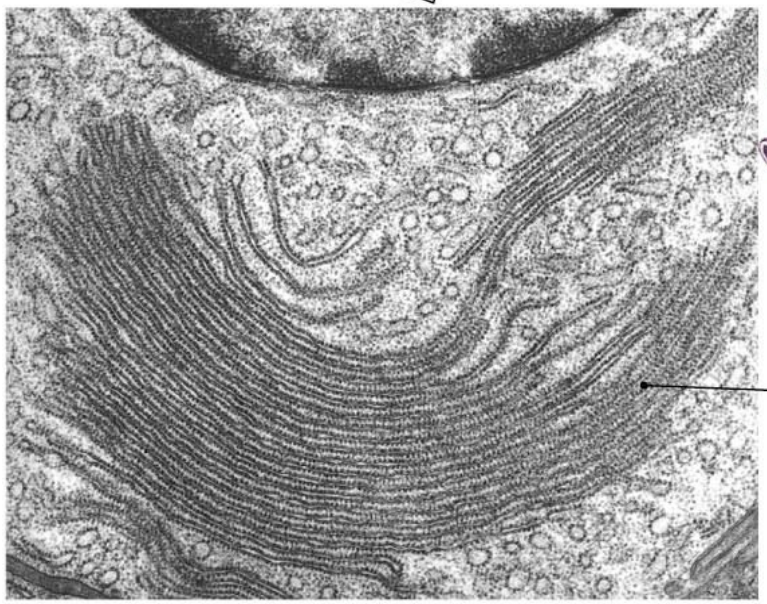
The **endoplasmic reticulum (ER)** is a network of interconnected membrane tubes that are a continuation of the outer nuclear membrane. **Rough endoplasmic reticulum** has a granular appearance due to rows of ribosomes dotting its cytoplasmic surface. **Smooth endoplasmic reticulum** lacks ribosomes and appears as smooth membrane tubes. The rough ER is the main site of protein synthesis. The smooth ER synthesizes lipids and, in some cells, concentrates and stores calcium ions.



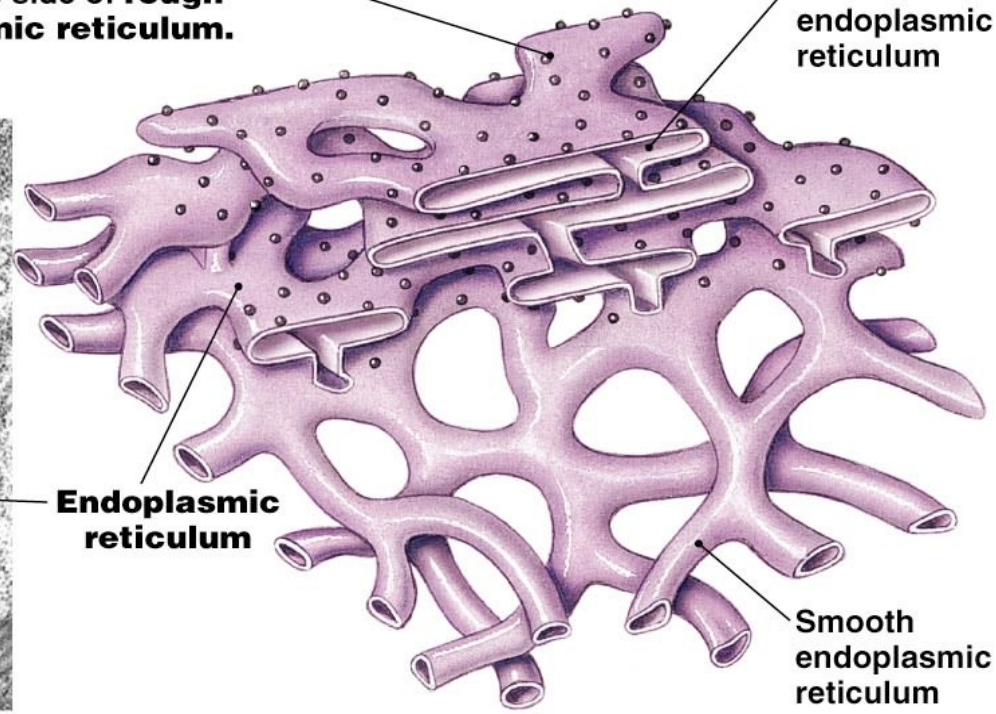


Ribosomes are attached to cytosolic side of **rough endoplasmic reticulum.**

Lumen of endoplasmic reticulum

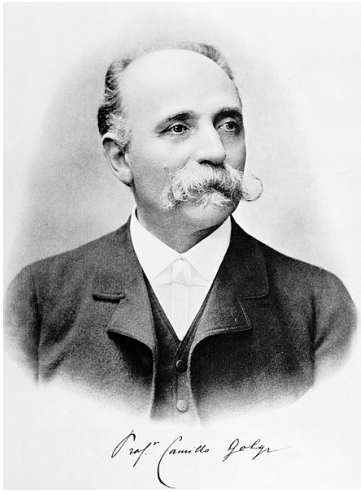


Endoplasmic reticulum



Smooth endoplasmic reticulum

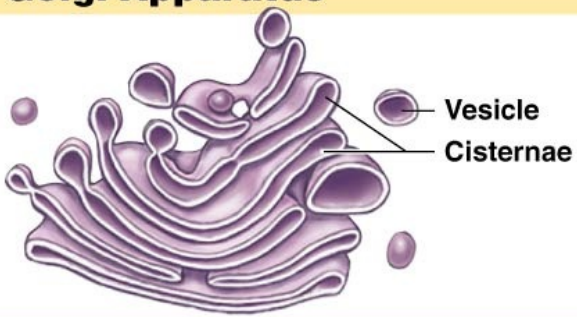
Golgi Bodies



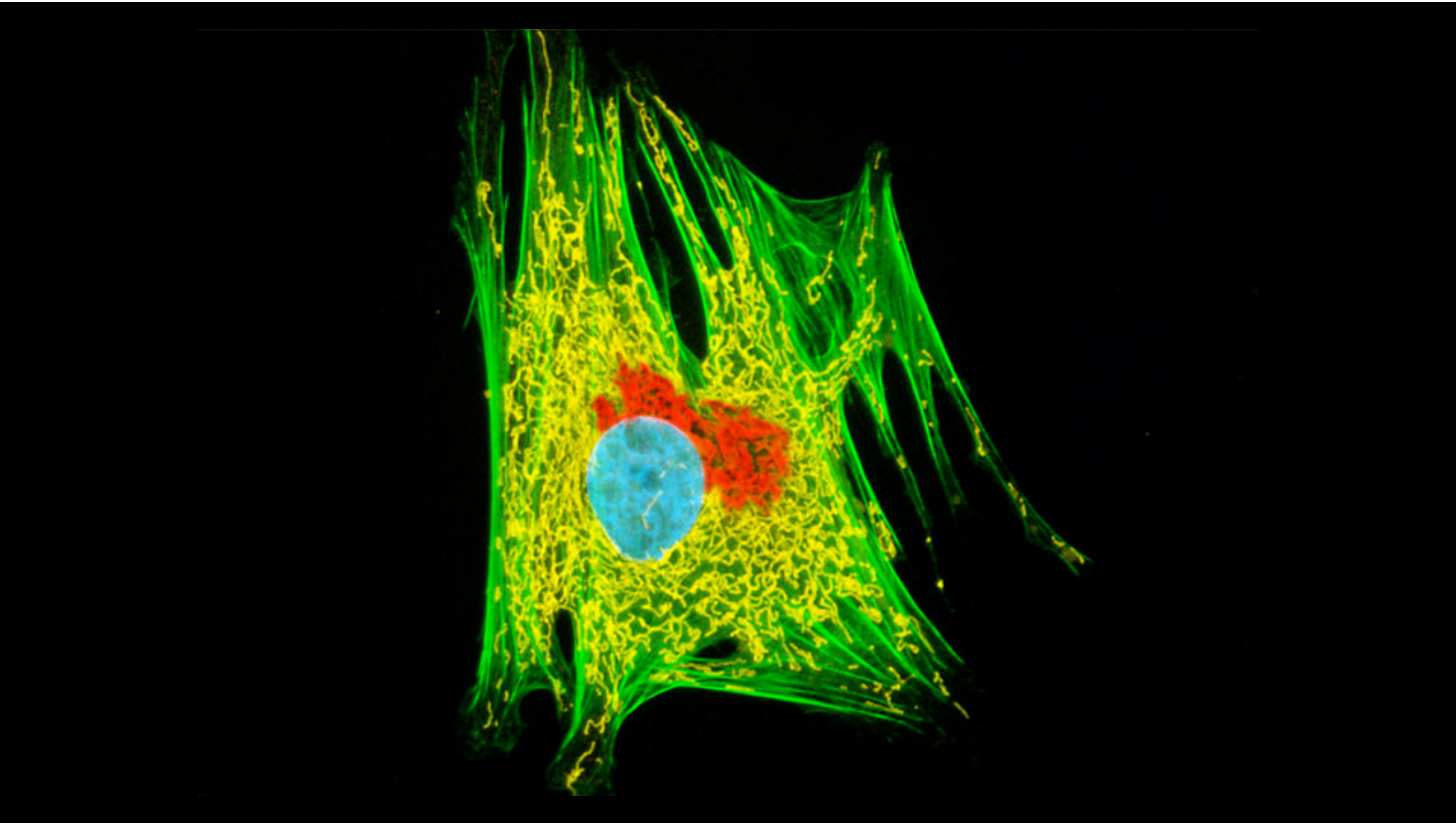
Camillo Golgi
University of Pavia
Neurological Pathology
1843 - 1926

- Golgi Bodies
  - "Postal Annex" of the cell

(h) Golgi Apparatus

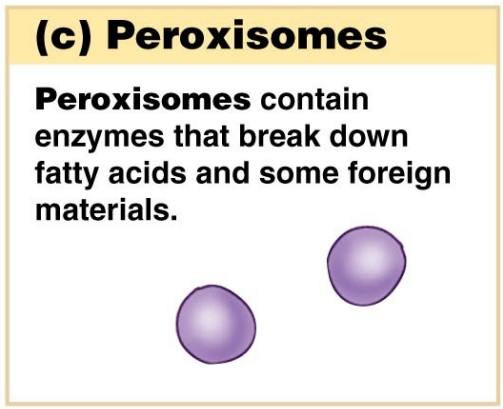


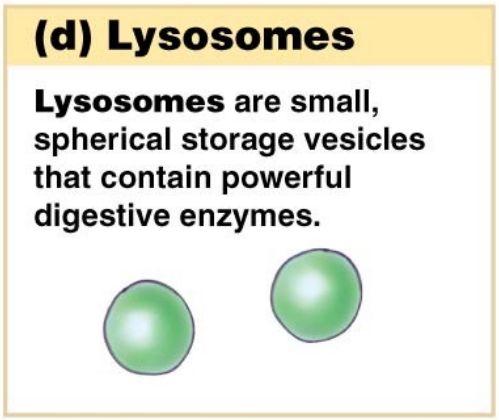
The **Golgi apparatus** consists of a series of hollow curved sacs called **cisternae** stacked on top of one another and surrounded by vesicles. The Golgi apparatus participates in protein modification and packaging.



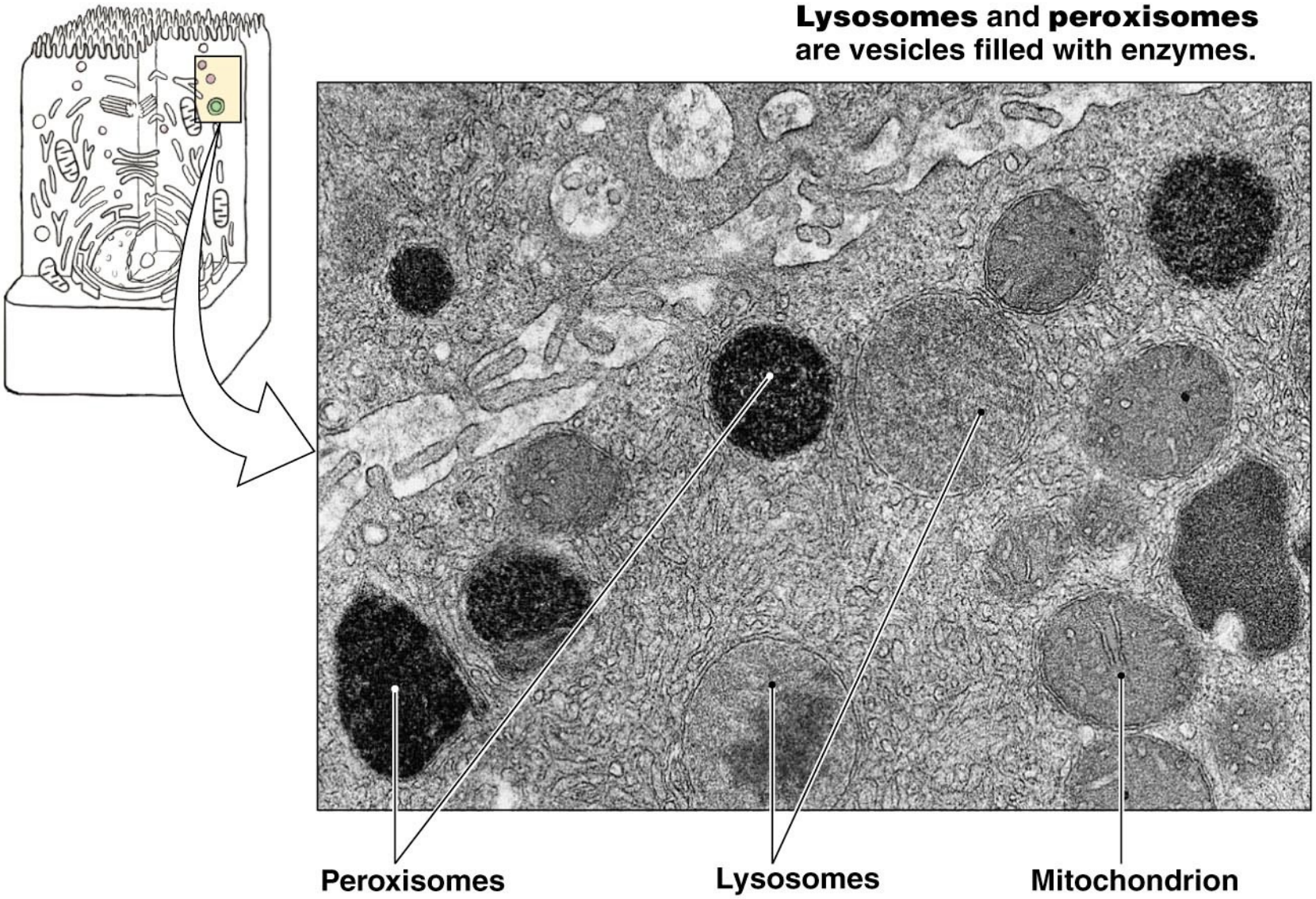
Waste and Recycling

- Lysosomes and Peroxisomes
  - Help to digest food, destroy foreign particles, recycle parts (autophagy)
  - What cell types would need a lot of these?

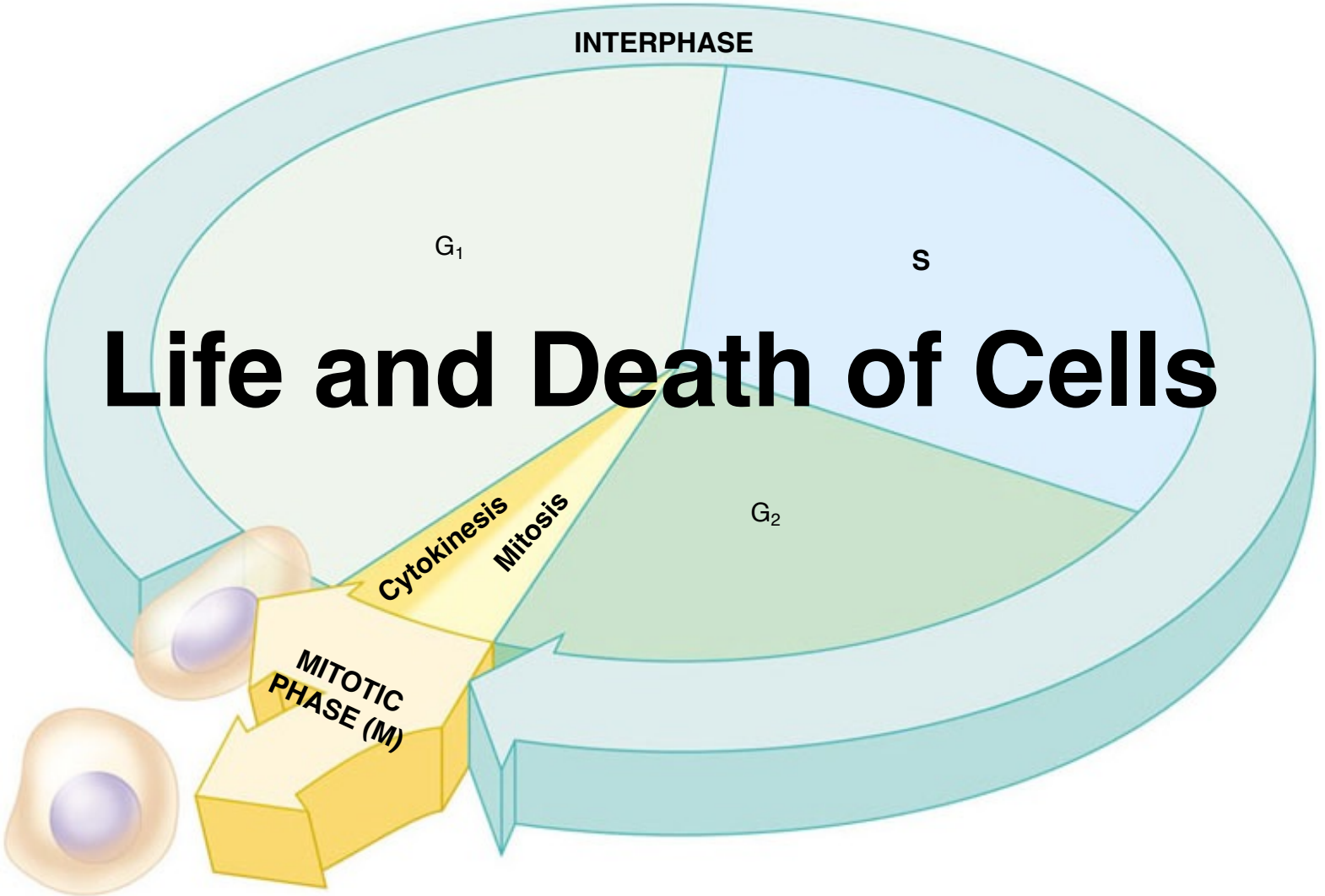




Lysosomes and **peroxisomes** are vesicles filled with enzymes.

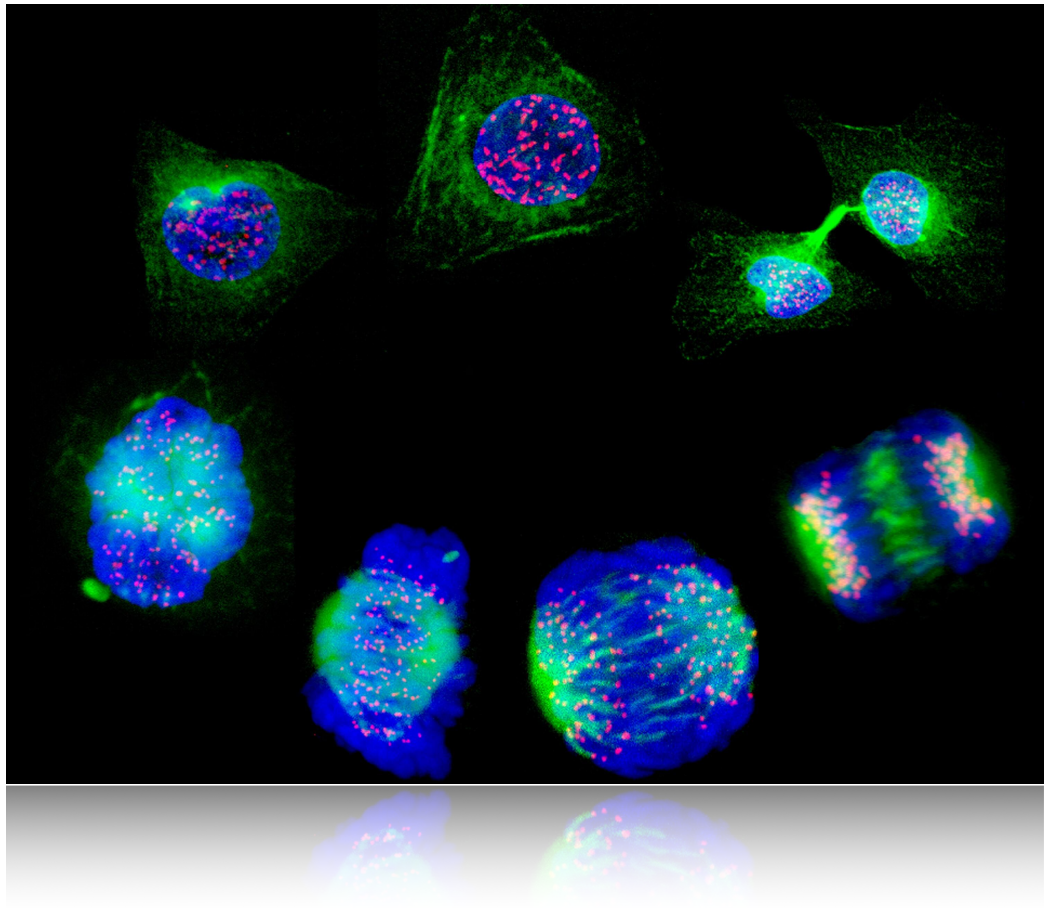


Life and Death of Cells



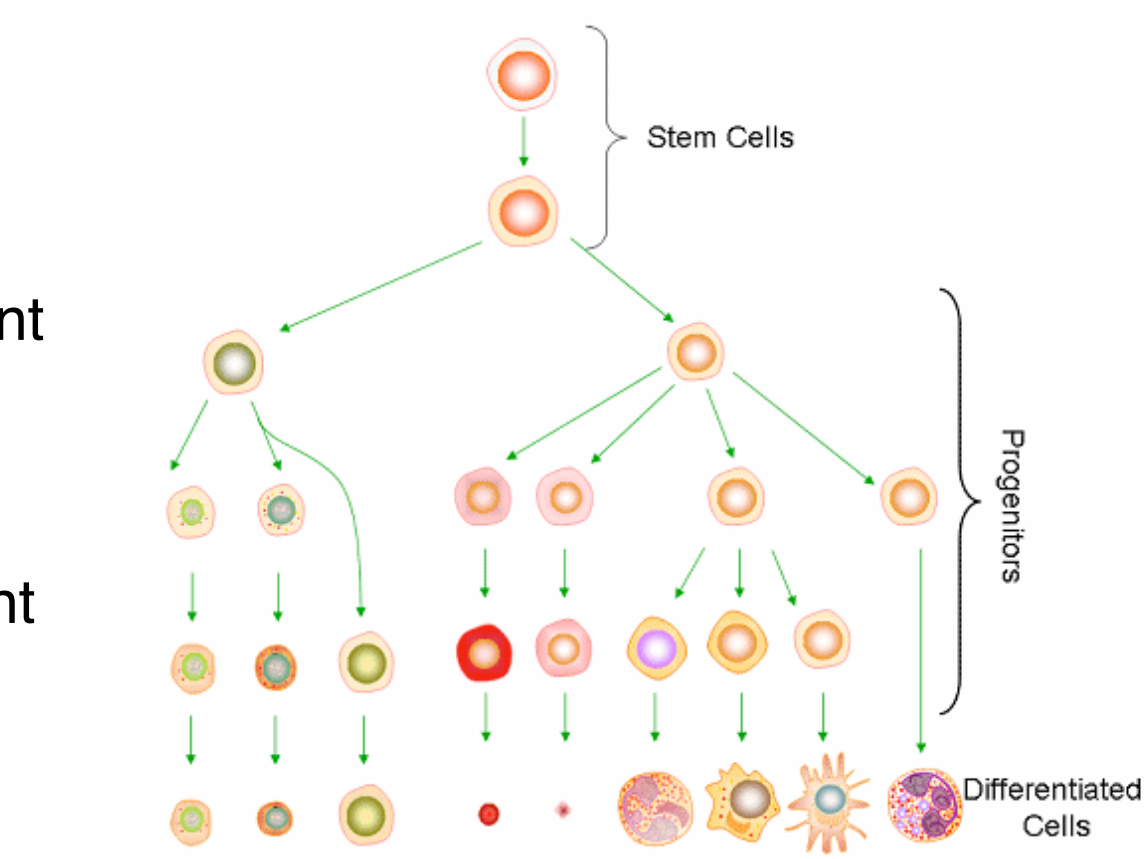
The Life and Death of Cells

- HOW do we have so many different types of cells?
- How do cells die?
- How do cells know WHEN to divide?
- What happens when things go wrong?



How Cells Become Differentiated

- There are 2 possibilities:
  - Different cells have different DNA
  - Different cells have the same DNA but use different parts of it

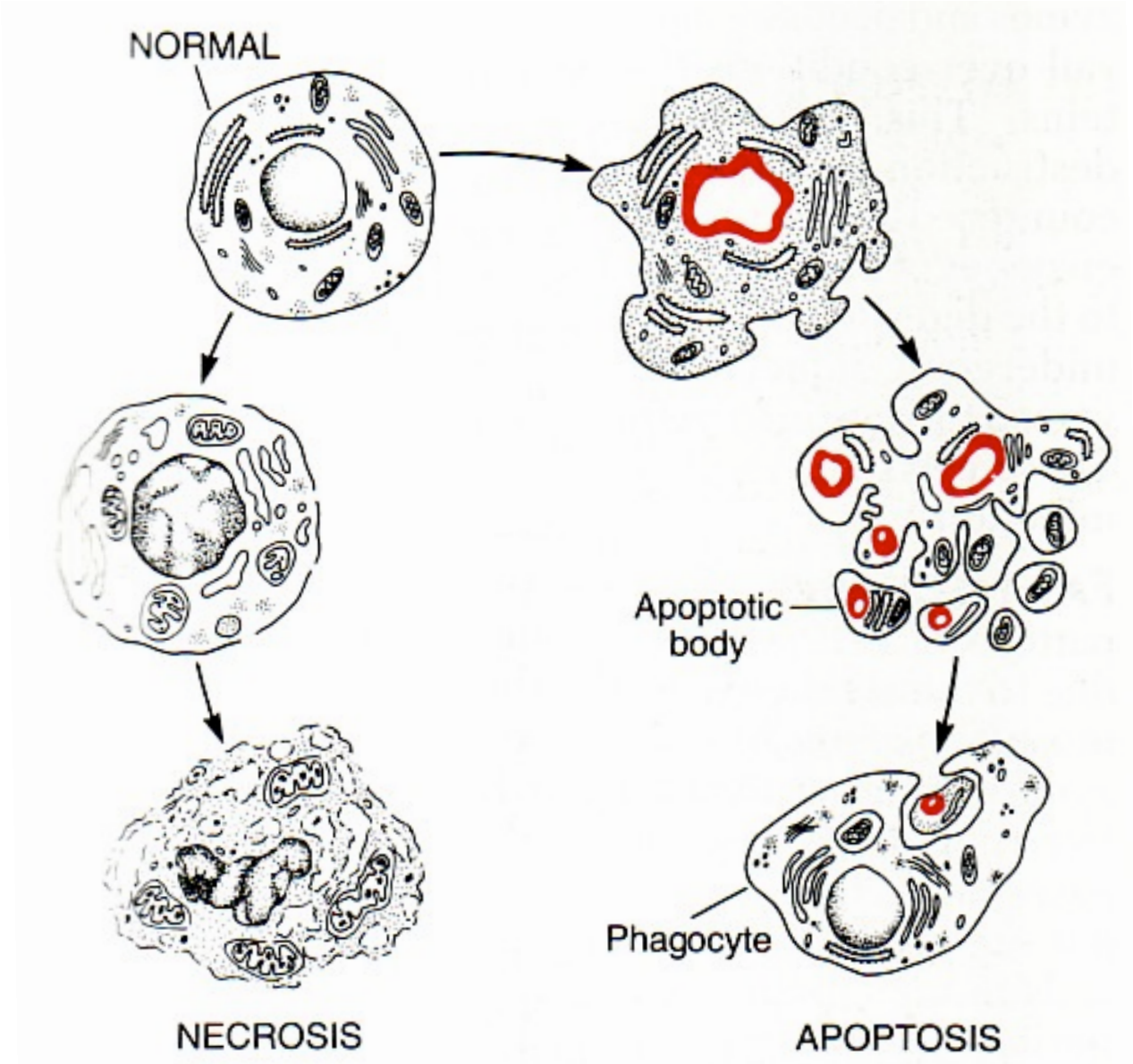


How Cells Die

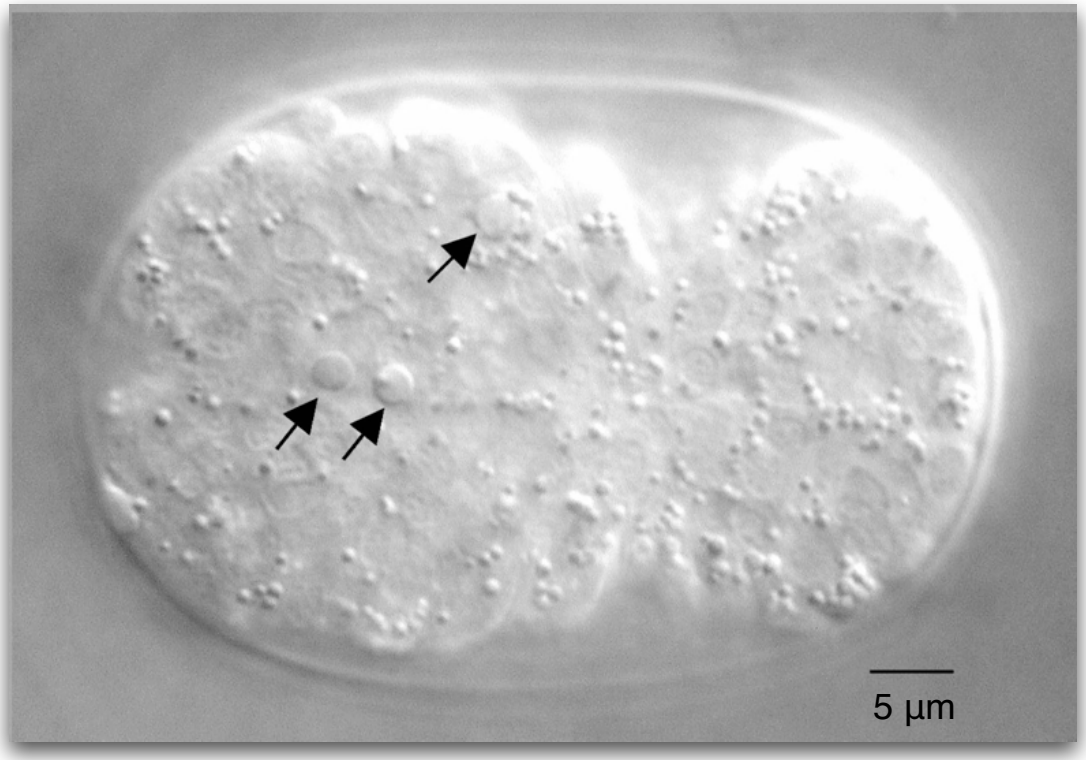
- Cellular necrosis
- Apoptosis - Programmed Cell Death
    - Cells are pre-programed for apoptosis
    - Signaling molecules are required to suppress apoptosis

from Greek *apoptōsis* ‘falling off,’ from *apo* ‘from’ + *ptōsis* ‘falling, a fall’

Necrosis	Apoptosis
cell swells	cell shrinks
organelles rendered non-functional	organelles remain intact
random DNA degradation	controlled DNA degradation
cell membrane damaged, permeable	cell membrane remains intact
cell ruptures	apoptotic body formation
induction of inflammatory response	phagocytosis
occurs in large groups of cells	occurs in individual cells


NORMAL
Apoptotic body
Phagocyte
NECROSIS
APOPTOSIS

Apoptosis



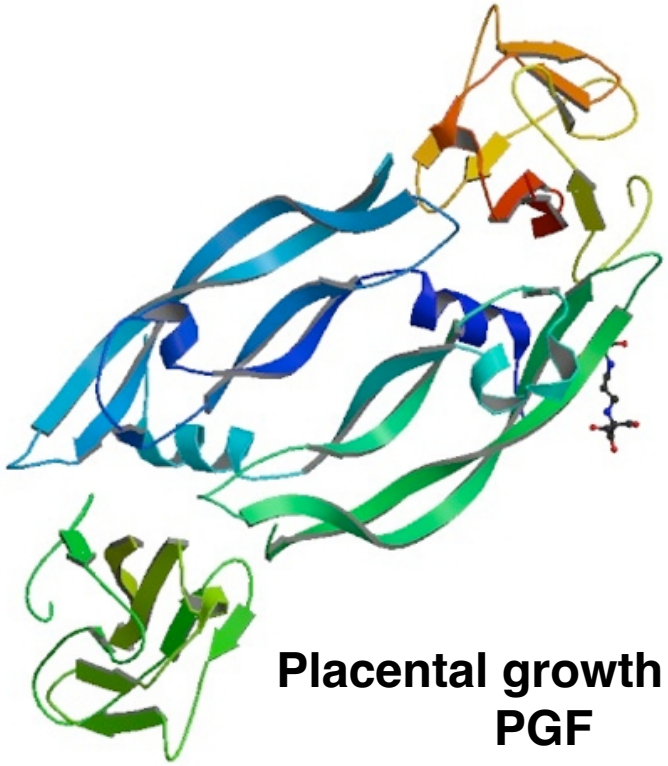
Embryonic apoptotic cells. Three cells indicated by arrows underwent programmed cell death and exhibit a refractile, raised-button-like appearance.

When Do Cells Divide

- Anchorage Dependence
  - Most cells “like or need” to be attached to something in order to go through mitosis

When Do Cells Divide

- Growth Factors
  - Proteins produced by cells to induce mitosis in their neighbors

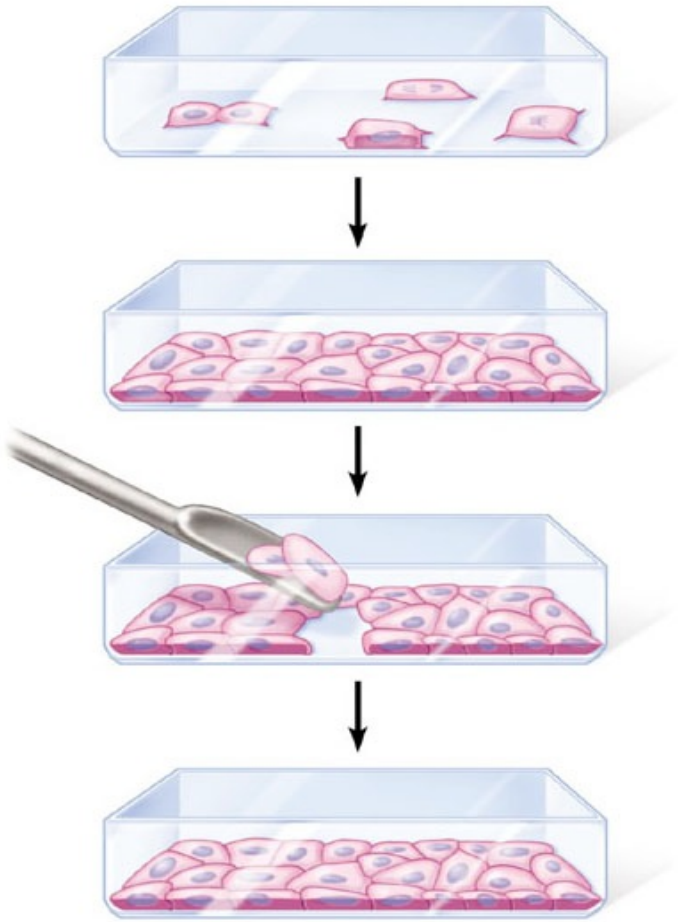


Placental growth factor
PGF

When Do Cells Divide

- Contact Inhibition
  - Cells inhibit each other's growth when they contact neighbors or a barrier

An experiment demonstrating density-dependent inhibition, using animal cells grown in culture

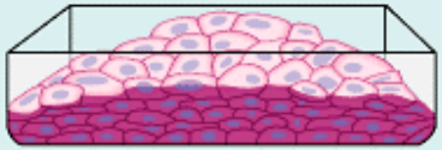


Cells anchor to dish surface and divide.

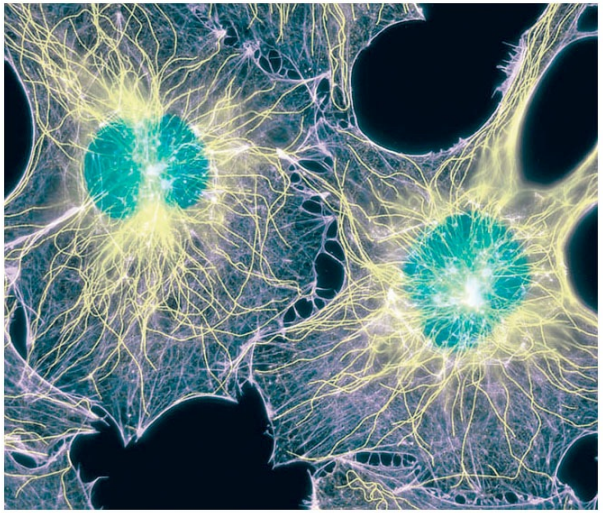
When cells have formed a complete single layer, they stop dividing (density-dependent inhibition).

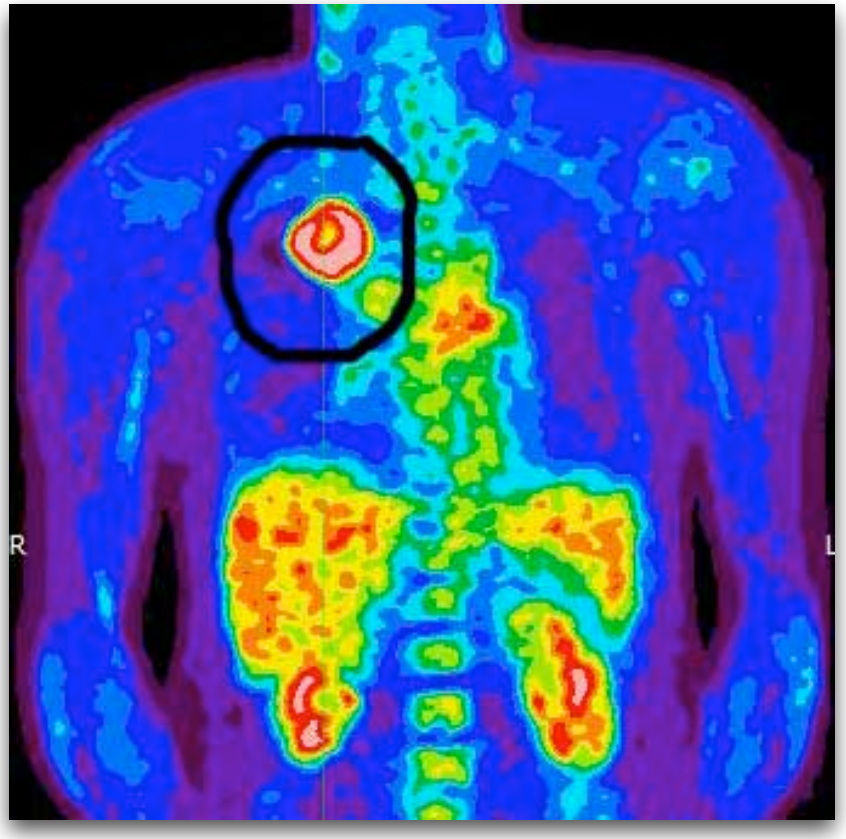
If some cells are scraped away, the remaining cells divide to fill the dish with a single layer and then stop (density-dependent inhibition).

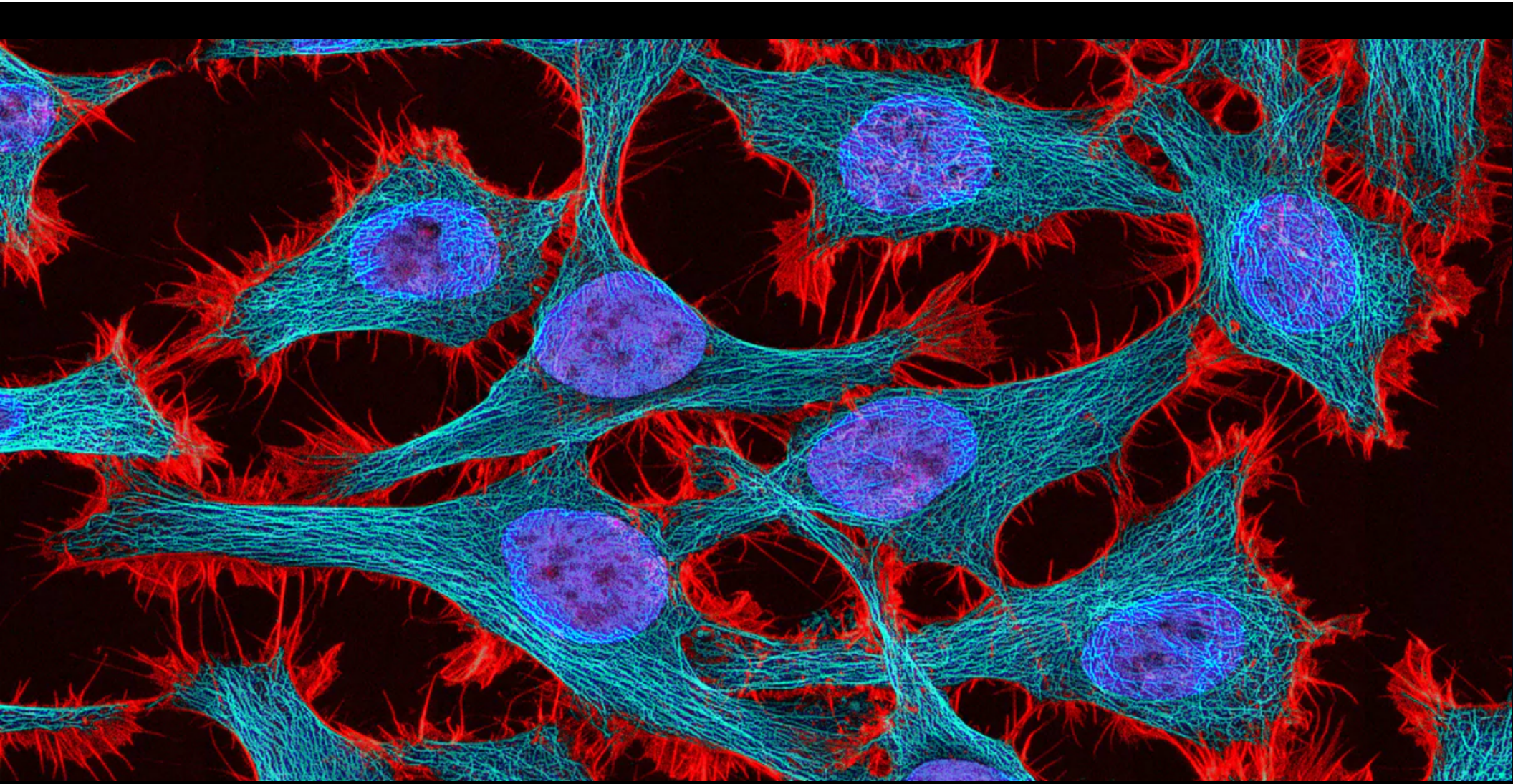
When Contact Inhibition is Lost



Cancer cells do not exhibit anchorage dependence or density-dependent inhibition.







HeLa cells visualized with fluorescent microscopy

Henrietta Lacks

Statue of Henrietta Lacks unveiled at University of Bristol

Press release issued: 4 October 2021

A life-size bronze statue of Henrietta Lacks, a Black American woman whose cells were the first ever to survive and multiply outside the body, and whose use changed the course of modern medicine, has been unveiled at the University of Bristol by members of her family to honour the 70th anniversary of her cells first being used.

The Lacks Family and artist Helen Wilson-Roe with the statue installed today in Royal Fort Gardens
Image credit: University of Bristol

Her son Lawrence Lacks, who was 17 when his mother passed away, was joined by her grandson Alan Wilks and his wife Pam, granddaughter Jeri Lacks-Whye and great-granddaughters Victoria Baptiste and Veronica Robinson for the unveiling this afternoon – Monday 4 October 2021.

HeLa Cells and SARS-CoV-2

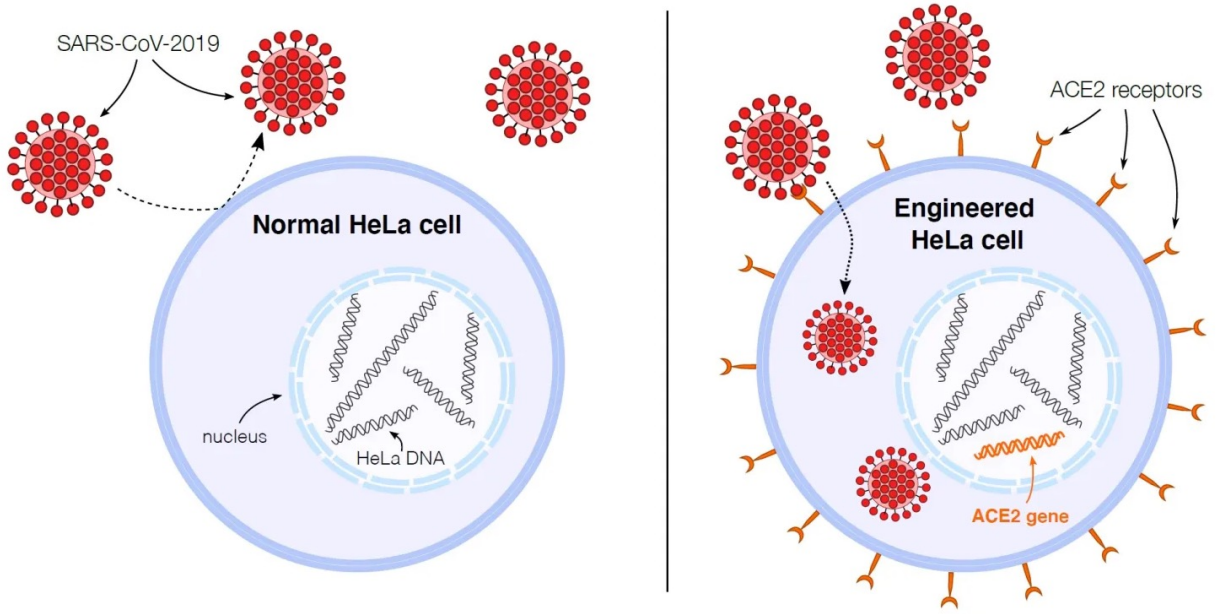
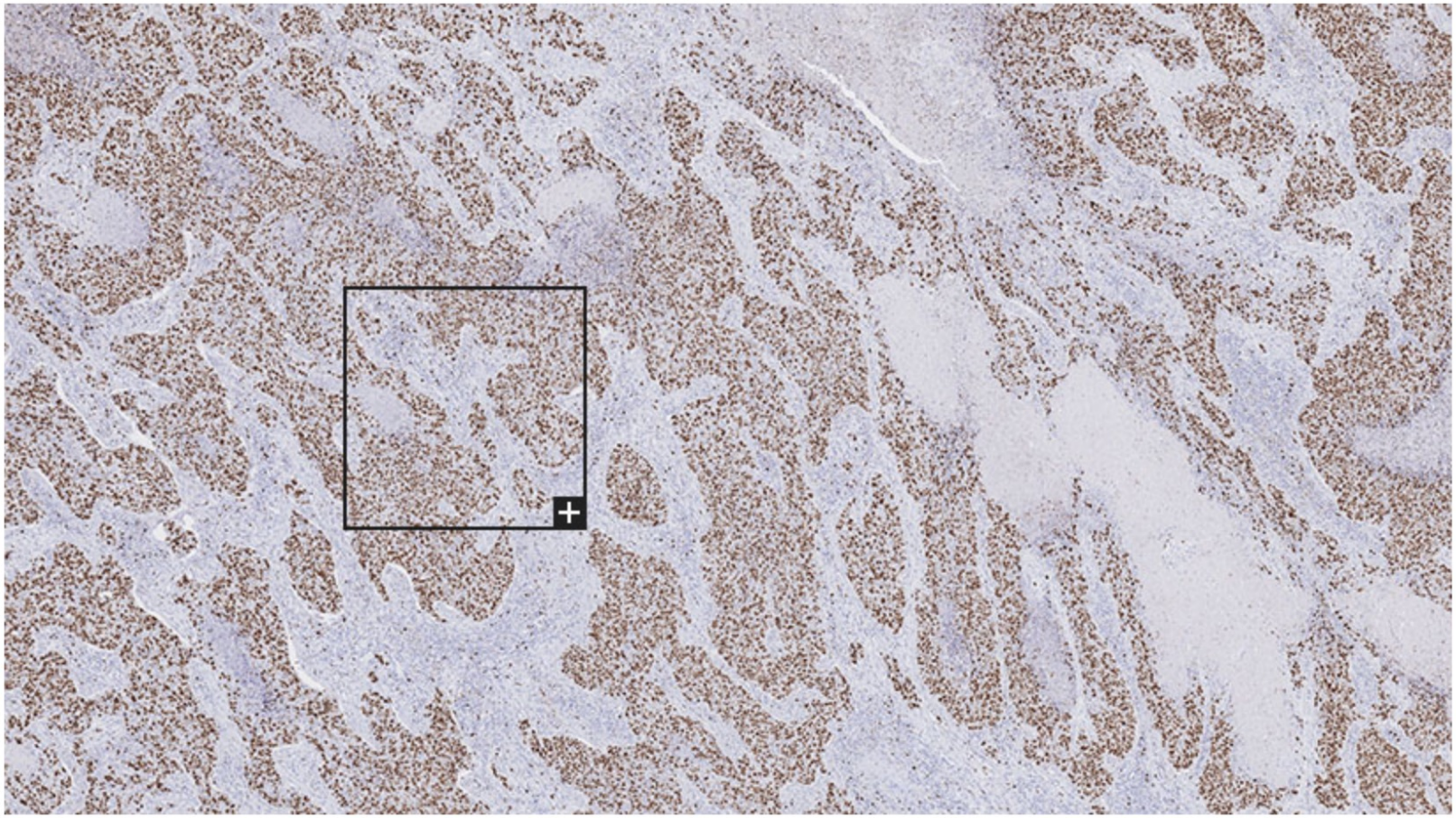


Figure 2: ACE2 receptors decorate the surface of HeLa cells to promote infection.
HeLa cells do not naturally display high levels of ACE2 proteins on their surface, preventing efficient infection by SARS-CoV-2 particles. However, when researchers engineer HeLa cells to display the ACE2 protein, the viral particles gain entry into the cells and begin their cycle of infection.

Cell Cycle Problems...

- Cells that divide when they shouldn't
- Cells that don't die when they should
  - We now have many tools to detect them, including markers for proteins that are expressed only during the M phase



Lung cancer (poorly differentiated squamous cell carcinoma) showing expression of the proliferation marker Ki-67 (MKI67) in tumor cells.

Ki-67 (MKI67) - General marker for proliferation

The MKI67 gene encodes a widely known yet functionally poorly characterized protein called Ki-67 that specifically labels the nuclei and chromosomes of cells actively undergoing proliferation, but is not detected in cells that are in resting G0-phase. Thus, Ki-67 is a very general marker for actively proliferating cells and this characteristic has been heavily exploited in both research and clinical work. It is commonly used to assess the proliferative activity in tumors, which may be a measure of aggressiveness in certain types of cancer.

Carcinogenesis

- DNA Mutations
  - Environmental Factors: radiation, tobacco, alcohol, radon, asbestos, etc.
  - Random somatic mutations
  - Random germ line mutations
    - Genetic predisposition

Carcinogenesis

- Infectious Agents
  - Viral
    - HPV: cervical cancer
    - Hepatitis: liver cancer
  - Bacterial
    - *H. pylori*: stomach cancer

RESEARCH INVESTORS & INDUSTRY ABOUT US WAYS TO GIVE Careers News

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Correlation is not (necessarily) causation

Or, how we know herpes doesn't cause cervical cancer — and HPV does

FEBRUARY 13, 2020 · BY SABRINA RICHARDS / FRED HUTCH NEWS SERVICE

Untangling cause and effect from mere association can be difficult. Epidemiologists walk through how they assess the evidence.

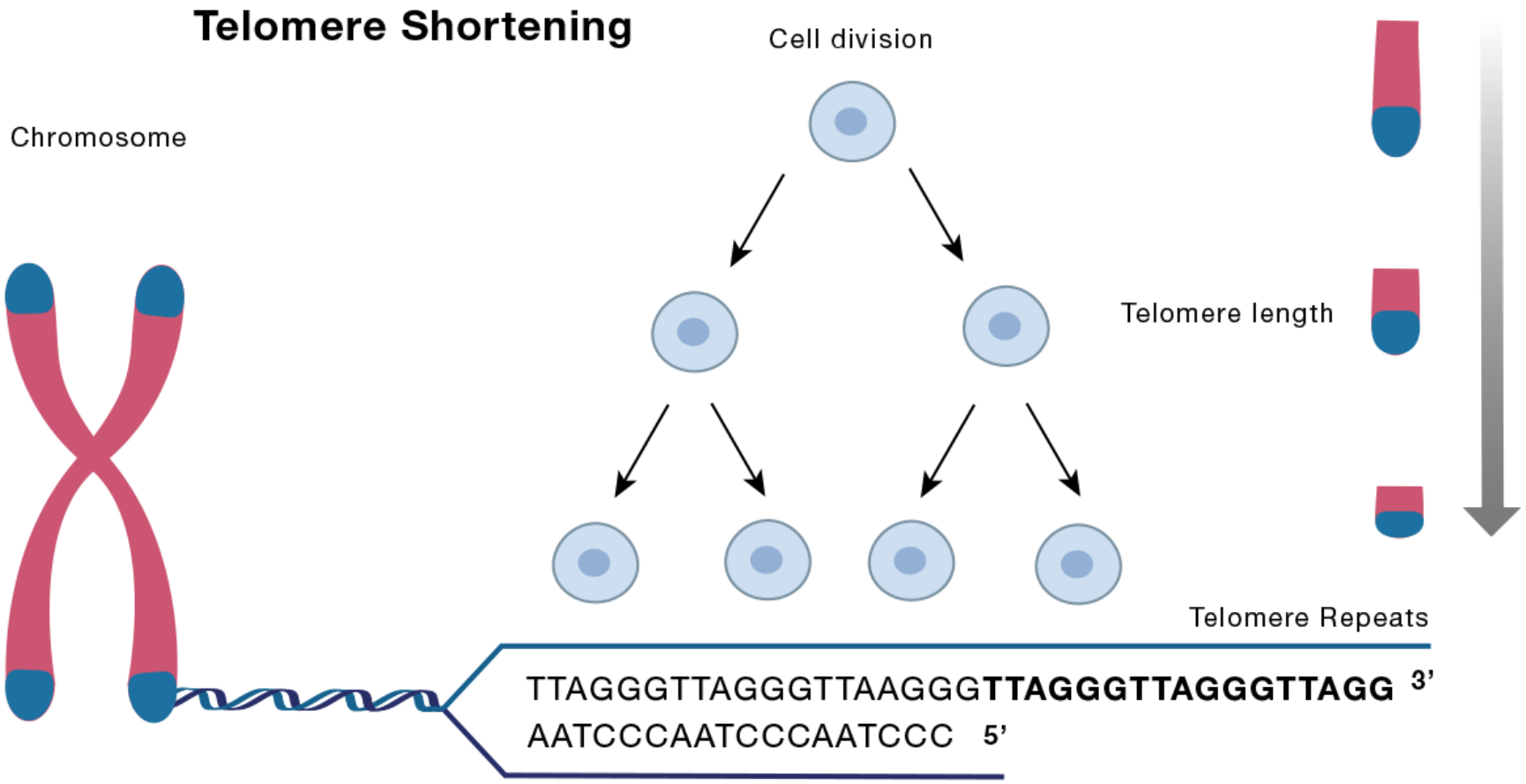
Getty Images

Hallmarks of (Almost All) Cancerous Cells

- **Self-sufficiency in growth signals** (oncogenes, transduction of normal genes: over-expression, amplifications and re-arrangements)
- **Insensitivity to growth-inhibitory signals** (mutations in tumor suppressor genes, TSGs)
- **Evasion of apoptosis** (FAS and FAS receptor, mutation of p53 which monitors DNA damage)

Hallmarks of (Almost All) Cancerous Cells

- **Sustained angiogenesis** (VEGF and FGF1 and FGF2 signal endothelial cell proliferation and growth of blood vessels)
- **Tissue invasion and metastasis** (little is known about these genes)
- **Limitless replicative capacity** through inactivation of telomeres


Telomere Shortening
Cell division
Chromosome
Telomere length
Telomere Repeats
TTAGGGTTAGGGTTAAGGGTTAGGGTTAGGGTTAGG 3'
AATCCCAATCCCAATCCC 5'