Cell Biology

Fall 2018/19

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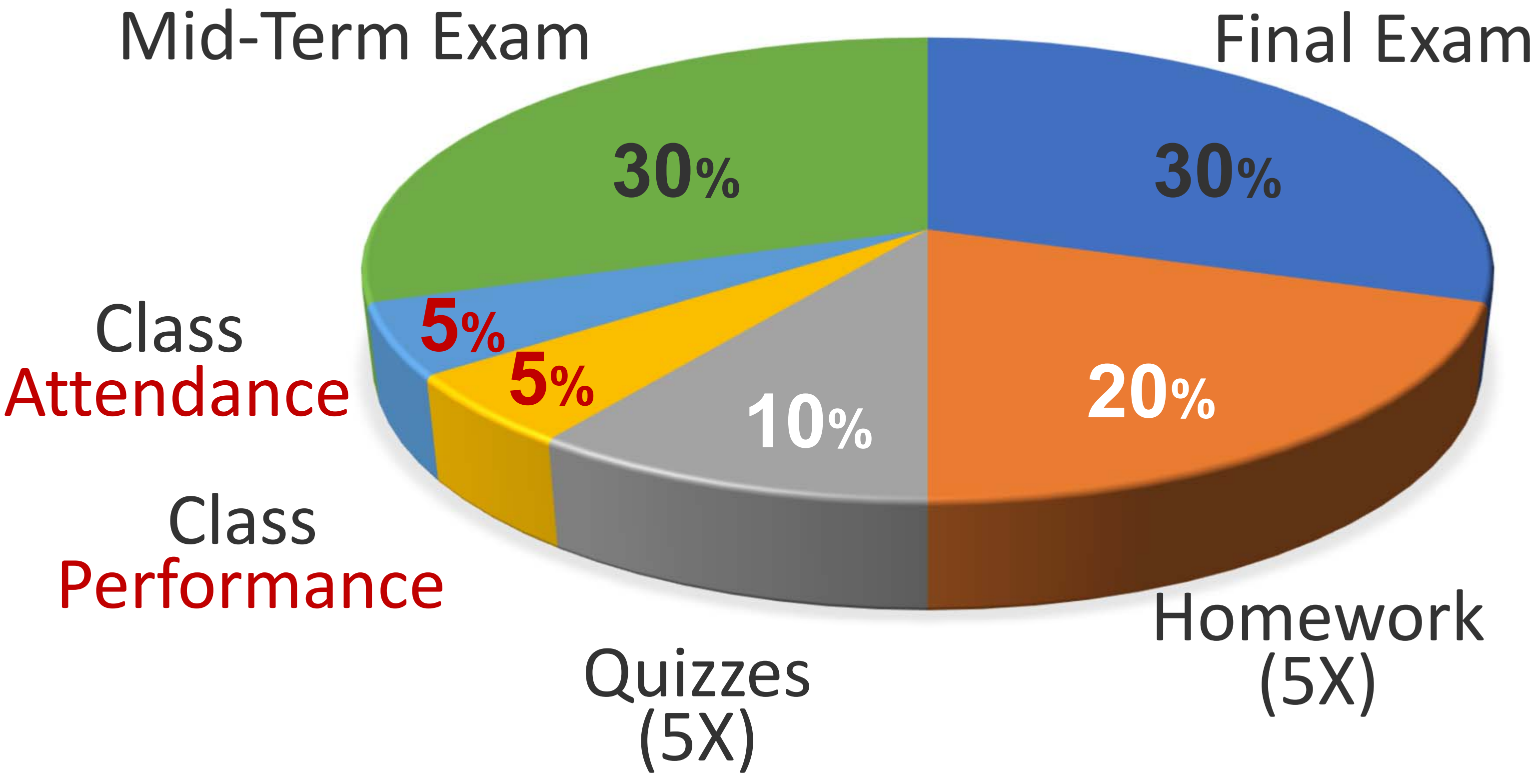
The organization of the class

The key to success:



Required for passing: 65%

The organization of the class

Three simple rules:

1. Class attendance is a must
   - timely appearance at 7:55 am
   - “signing-in” attendance list on arrival, before the lecture
   - “written excuse” for missed classes
2. Keep track with the class
   - rehearse each class immediately to prepare for the upcoming quizzes
   - hand in homework timely
3. Don’t be shy
   - don’t fear English language
   - ask questions, questions are welcome
   - participate actively

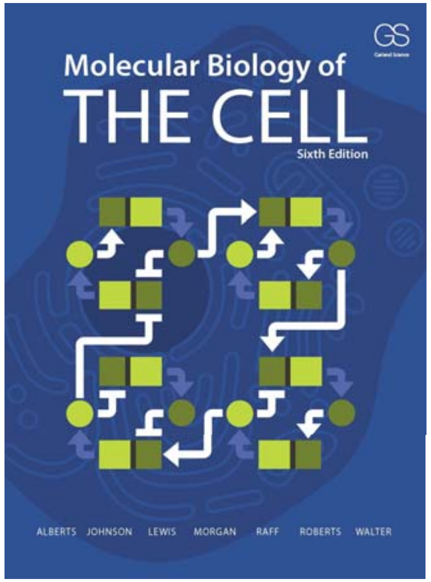
Southern University of Science and Technology
SUSTech

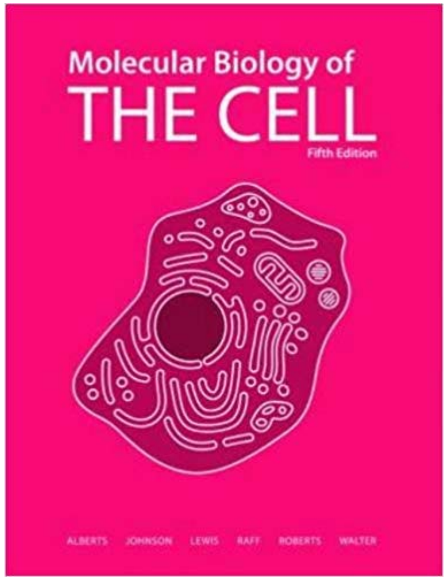
Cell Biology

- Tools -

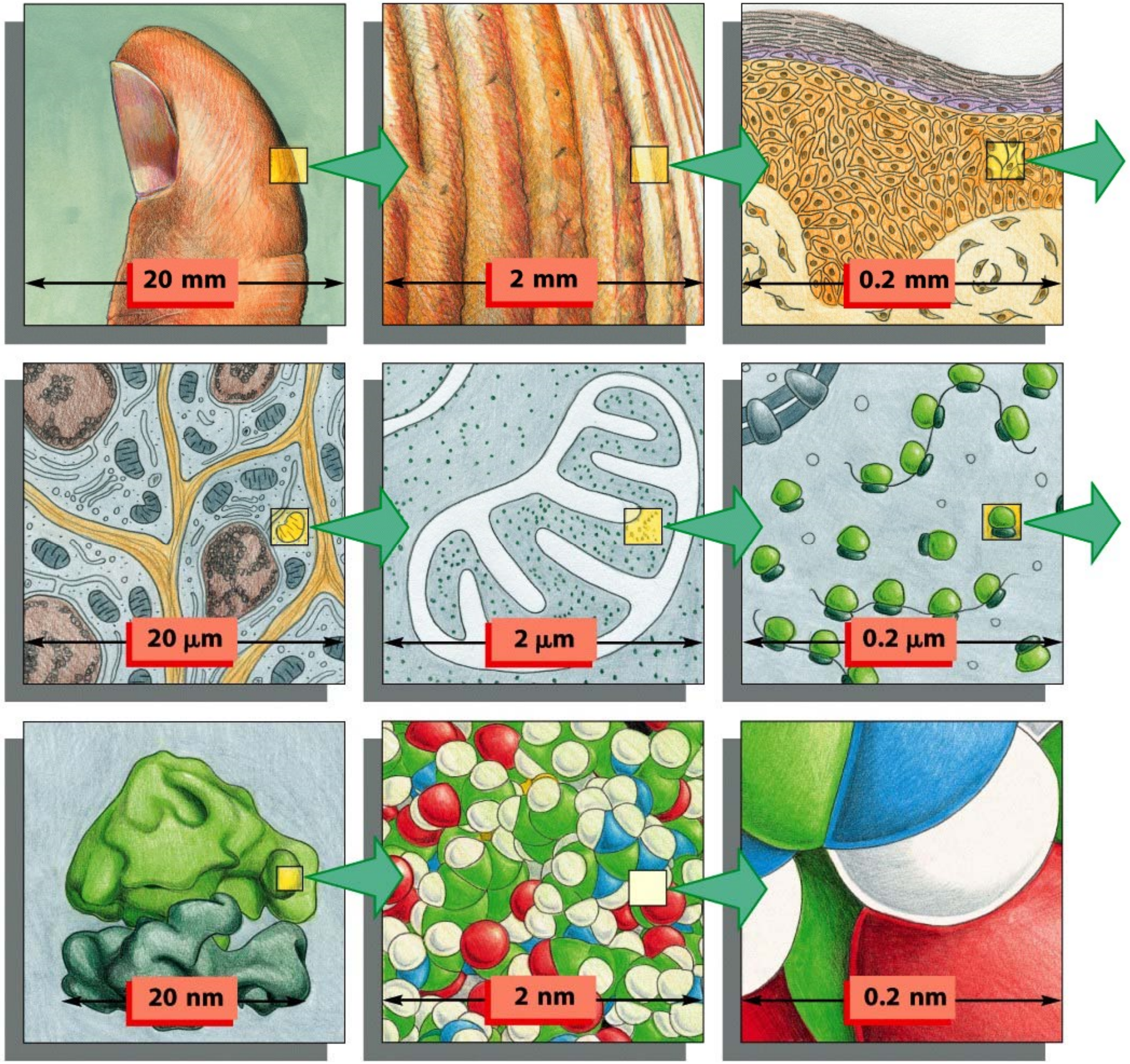
Textbook: **Molecular Biology of the Cell**

(Alberts et al., 6th/5th edition, Garland Science





Thoughts before we start: comparison of sizes



Physiology

Cell Biology

Biochemistry

Figure 1-9 Essential Cell Biology 3/e (© Garland Science 2010)

Cell Biology

- three questions -

What is it about?
What can we learn?
Why is it important?

What can cell biology tell us about longevity?

The mystery of longevity: a mouse versus a human

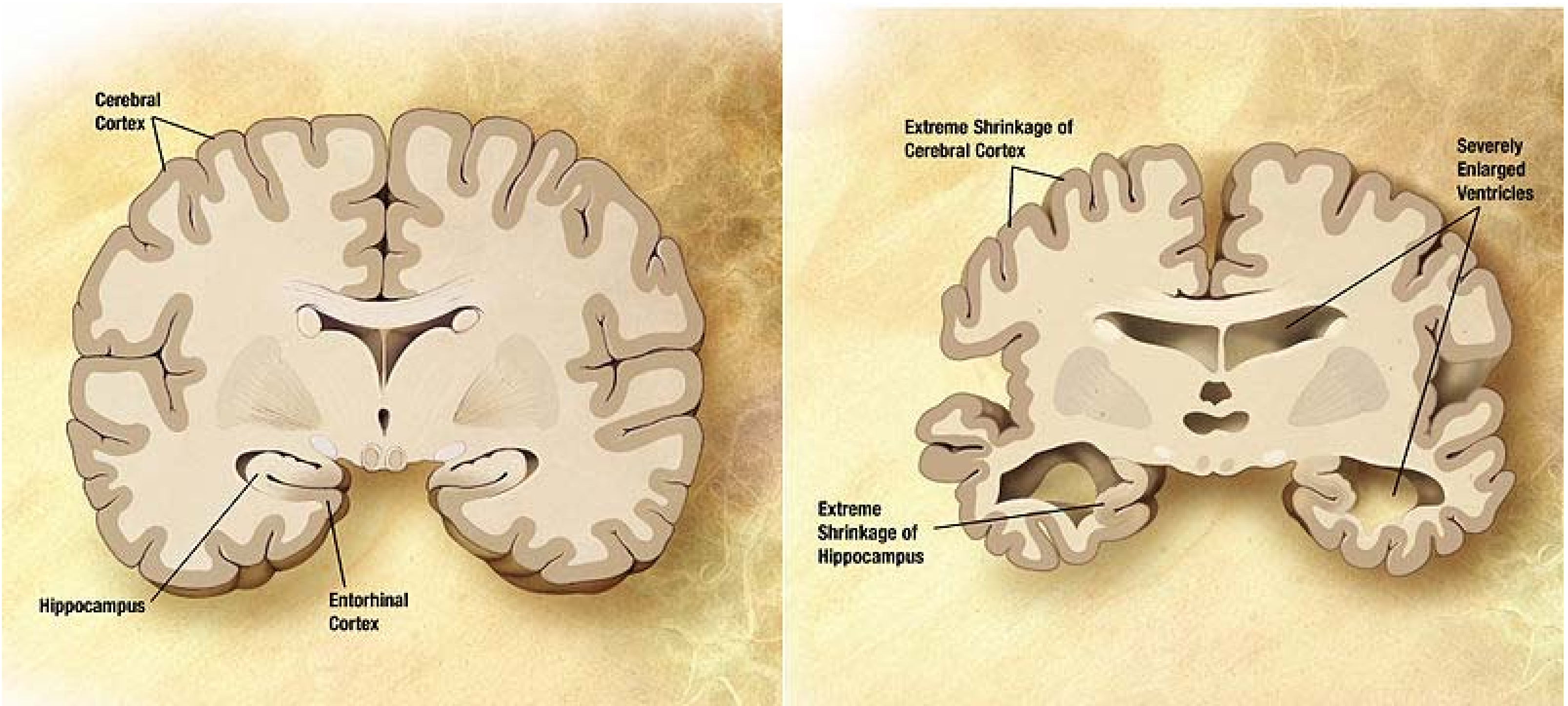
		Genome size	proteins	chromosomes
	**Live up to 2 years old**	3,421 million bp	22,085	20
	**Live up to 80 years old**	3,279 million bp	21,077	23

Over than 99% of human genes have homologs in mice, vice versa.

But what decides mice live a shorter life?

What can cell biology tell us about human diseases?

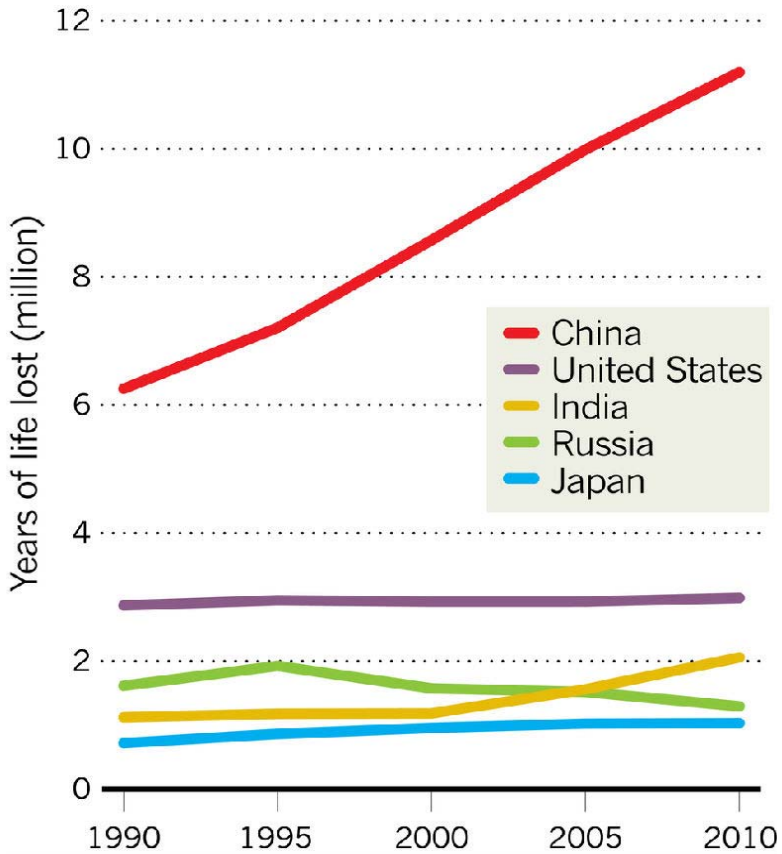
If we live up to 80 years, we might experience degenerative diseases



Cause of Alzheimer's disease remains a mystery, no cure yet…

What can cell biology tell us about premature mortality?

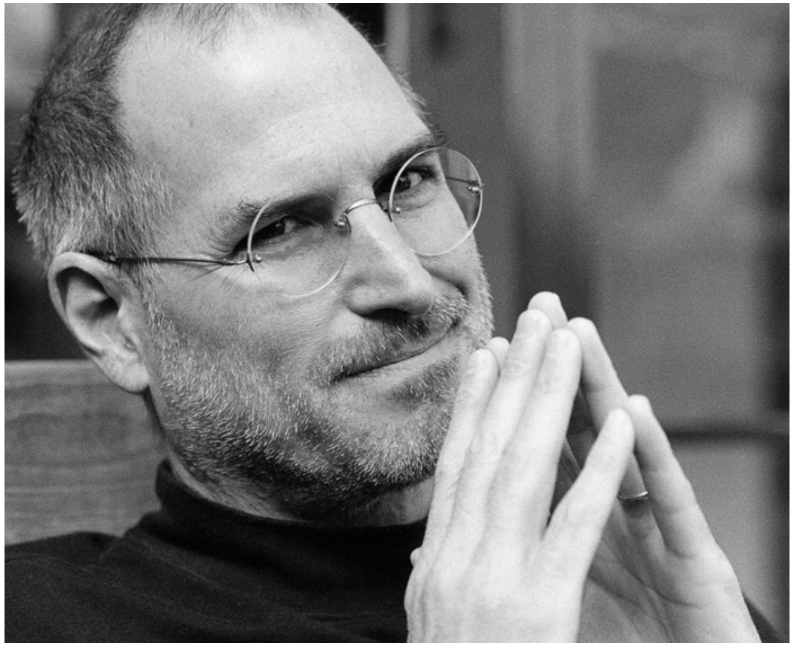
We might not live up to 80 years because of premature mortality.
Why is this worse in China compared to other countries?



Why do nearly 600,000 people die from lung cancer every year in China?

What can cell biology tell us about cancer?

Elephants vs. humans: Why don't elephants suffer from cancer?



How can elephants avoid cancer?

What can cell biology tell us about cancer?

The protein p53 protects cells from cancer

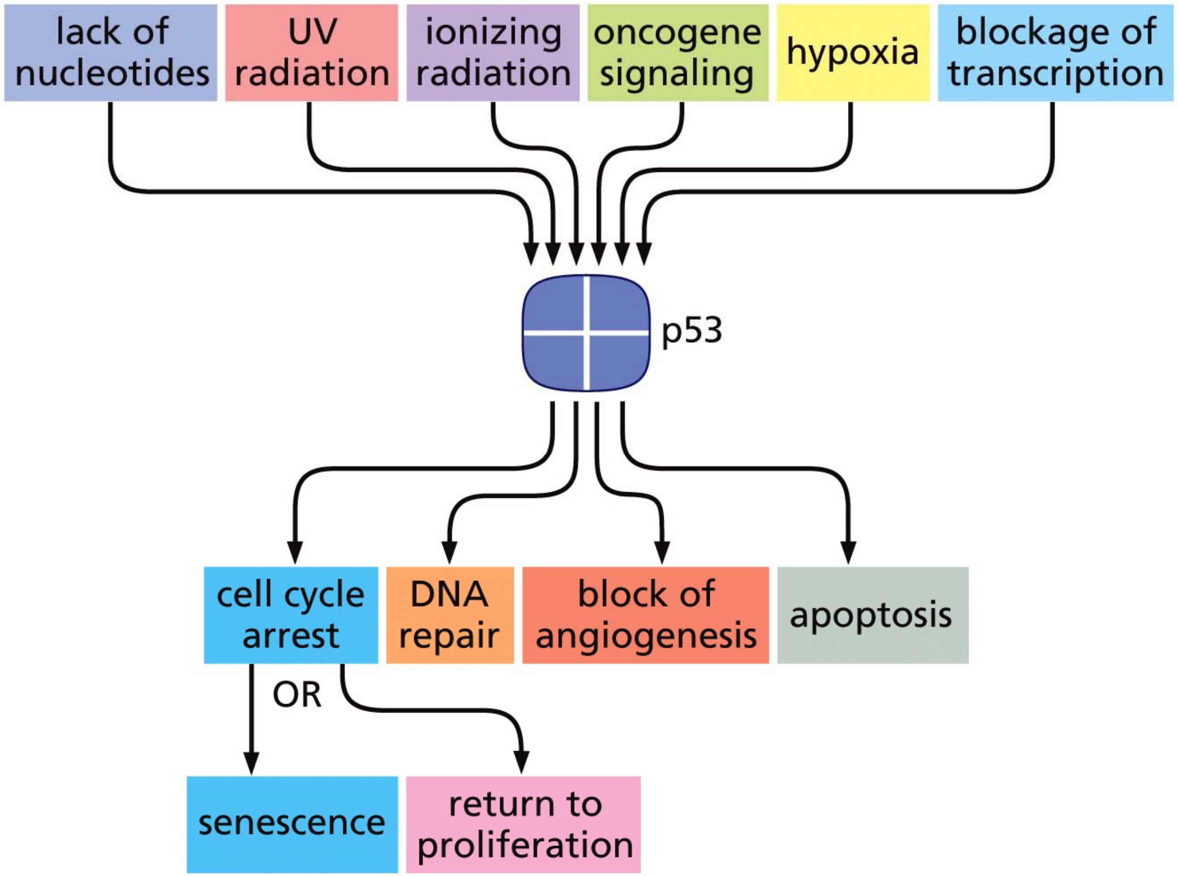


Figure 9.8 The Biology of Cancer (© Garland Science 2014)

How can one single protein protect cells from cancer progression?

What can cell biology tell us about new forms of therapies?

What about cell therapy?

Tissue-specific stem cells

Engineered immune cells

The ultimate solution?

CD19-specific chimeric antigen receptor (CAR) T cell therapy



Emily Whitehead

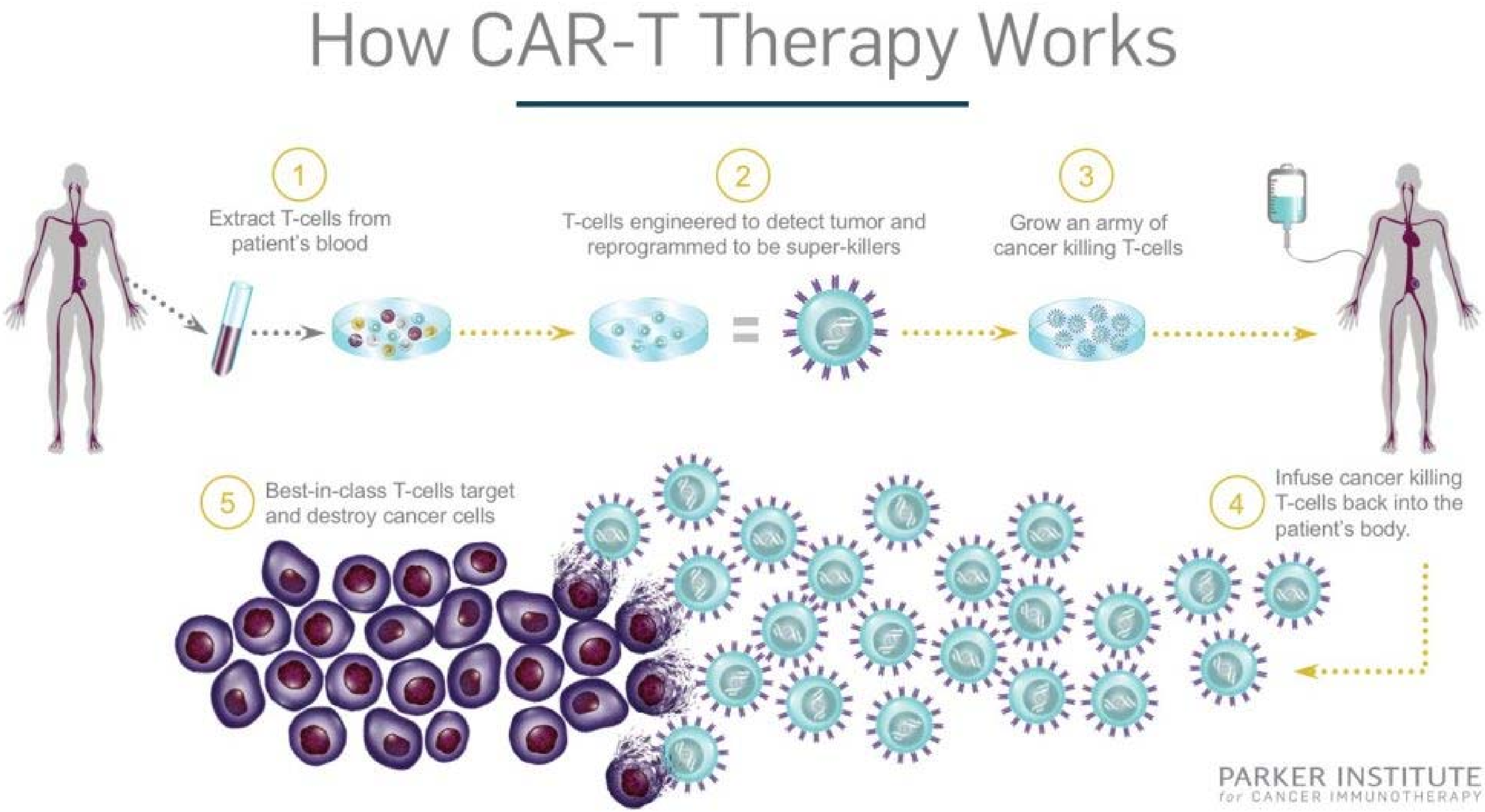
A case of how these cells cure ALL

03/2013, New England Journal of Medicine

http://emilywhitehead.com/

What can cell biology tell us?

Development of new drugs and medical approaches



What can cell biology tell us?

Does medicine grow?

Molecular pharming: the production of vaccines

... only vaccines?

What can cell biology tell us?

Does medicine grow?

Plantibodies

I am not sick, do I need cell biology?

What can cell biology tell us?

The most important question: What will we eat tomorrow?

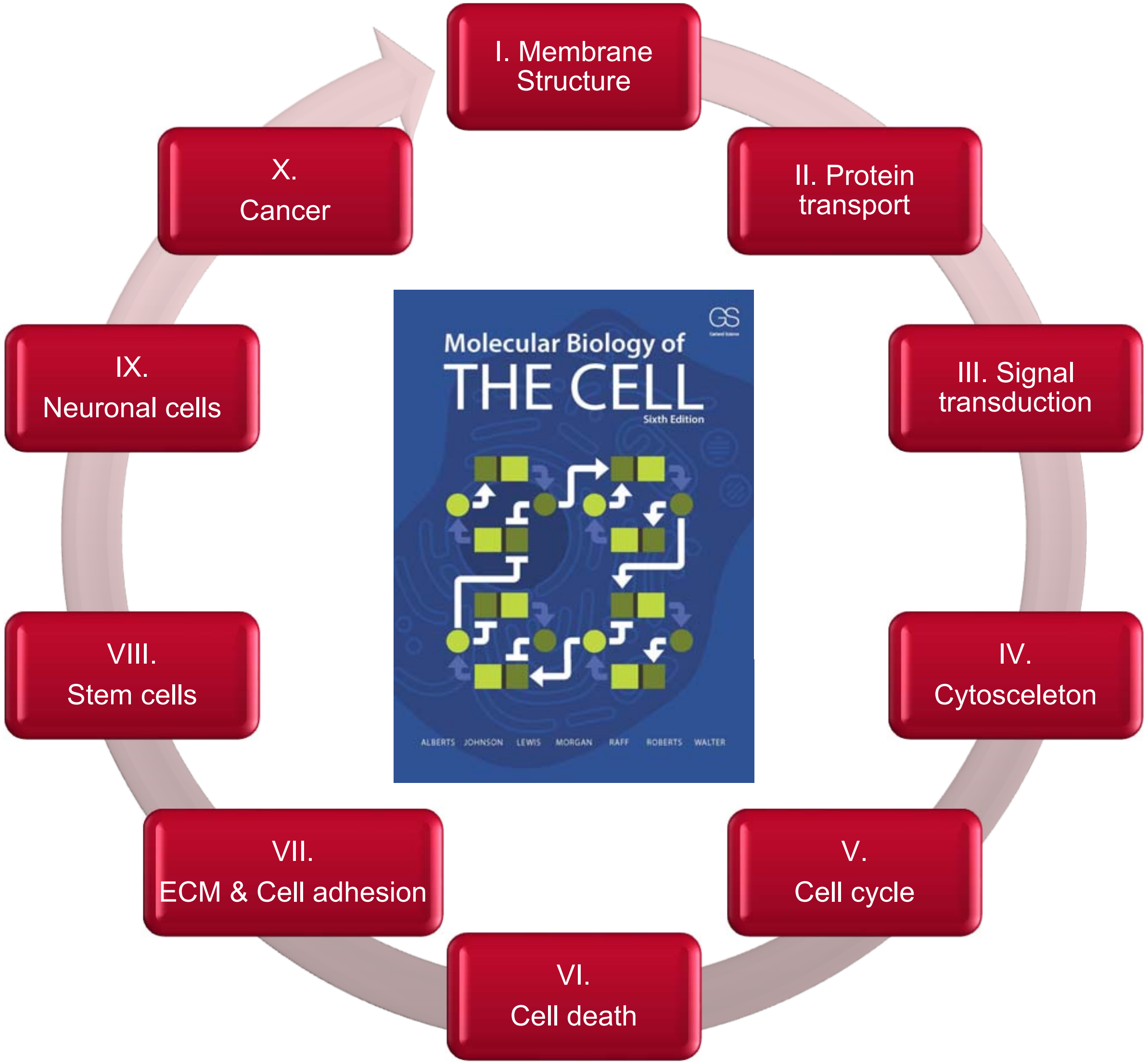
… and where will it grow?

What can cell biology tell us?

The most important question: What will we eat tomorrow?

… and where will it grow in an ever changing environment?

Structure and content of the course



Overview of lecture 1

Cells & cell biology

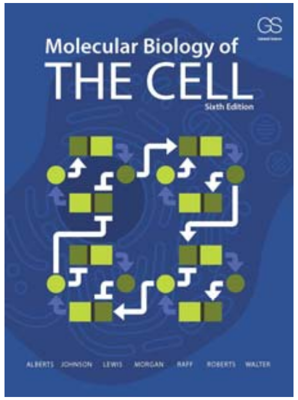
1.1 Cell theory

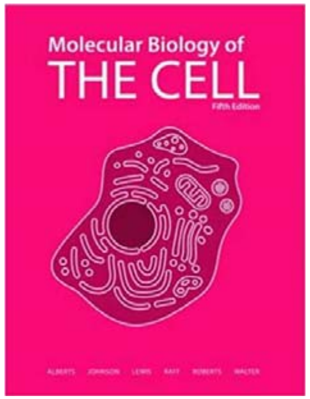
1.2 The differences between eukaryotic cells and prokaryotic cells

1.3 The constancy of all cells

1.4 How cells evolved

1.5 The use of model systems to study cell biology





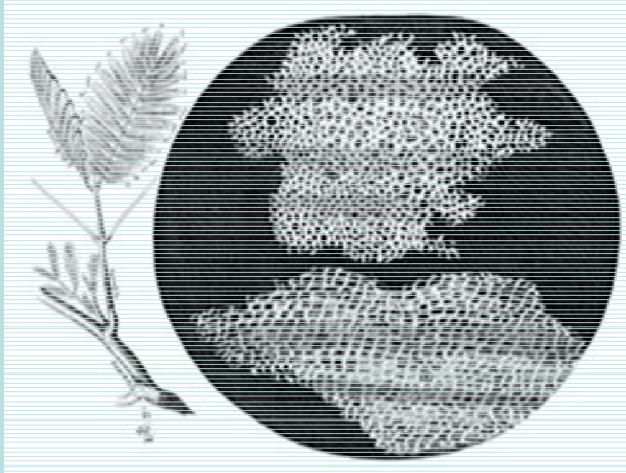
Chapter 1: Cells and Genomes

1.1 Discovery of cells

1665

Robert Hooke
1653-1703, England

In 1665, Robert Hooke saw a network of tiny box-like compartments that reminded him of a honeycomb…



… he called these little compartments "*cellulae*", a Latin term meaning little room.
Our present-day term therefore is: "**cell**".

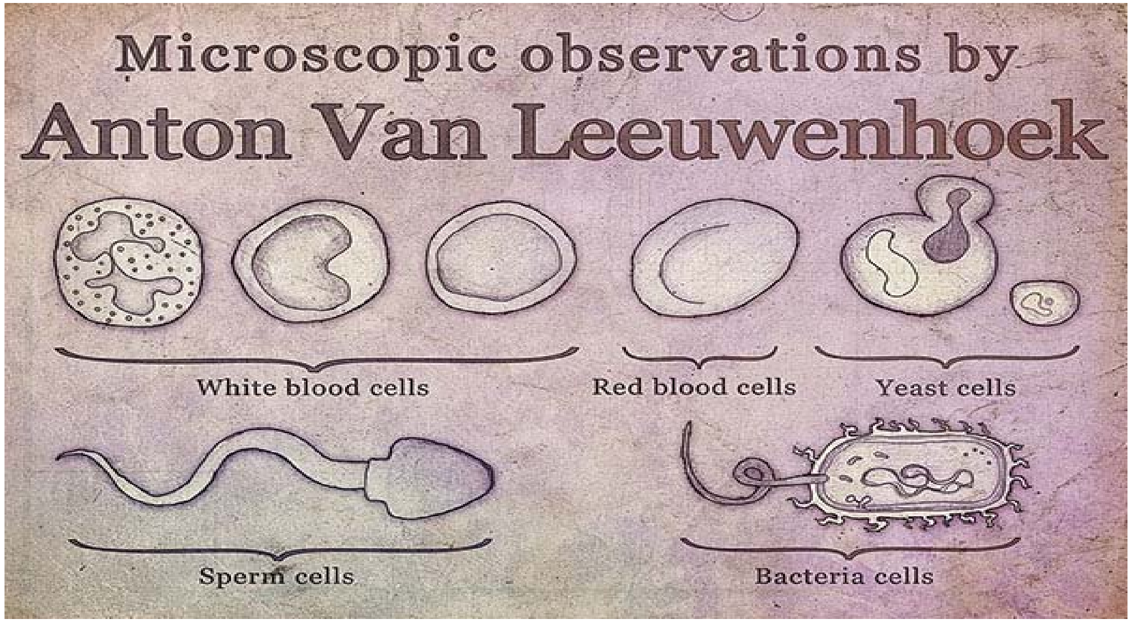
In fact, these were cell walls, left by dead cork cells…

Improvement of technology: The quality of lenses

~1670s

Antoni van Leeuwenhoek
1632-1723, Netherlands

As a good lens maker, Leeuwenhoek greatly **increased the resolution** of lenses.



Leeuwenhoek was the first to observe & describe single-celled organisms (“animalcules”).

First to record observations of muscle fibers, bacteria, spermatozoa and blood flow.

Actually, he was the first to observe live cells…

Matthias Schleiden & Theodor Schwann proposed the Original Cell Theory

1838-1839

M.J. Schleiden

German botanist
(1804-1881)

Theodor Schwann

German physiologist
(1810-1882)

Schleiden & Schwann systematically studied tissues of plants and animals under the microscope and showed：

1. Cells are the building blocks of all living things.

2. All cells have similar structure: nucleus and membrane.

Schwann is also famous for the discovery of nerve sheath cells : “Schwann” cells...

Cells derive from pre-existing cells

1855 Are cells from pre-existing cells or because in instinct it has vitalism?

Rudolf Virchow
(1821-1902)
German doctor

What is the origin of cells?

Rudolf Virchow proposed cells are from pre-existing cells:

Omnis cellula e cellula
("all cells (come) from cells"),

but there was no experimental proof, until...

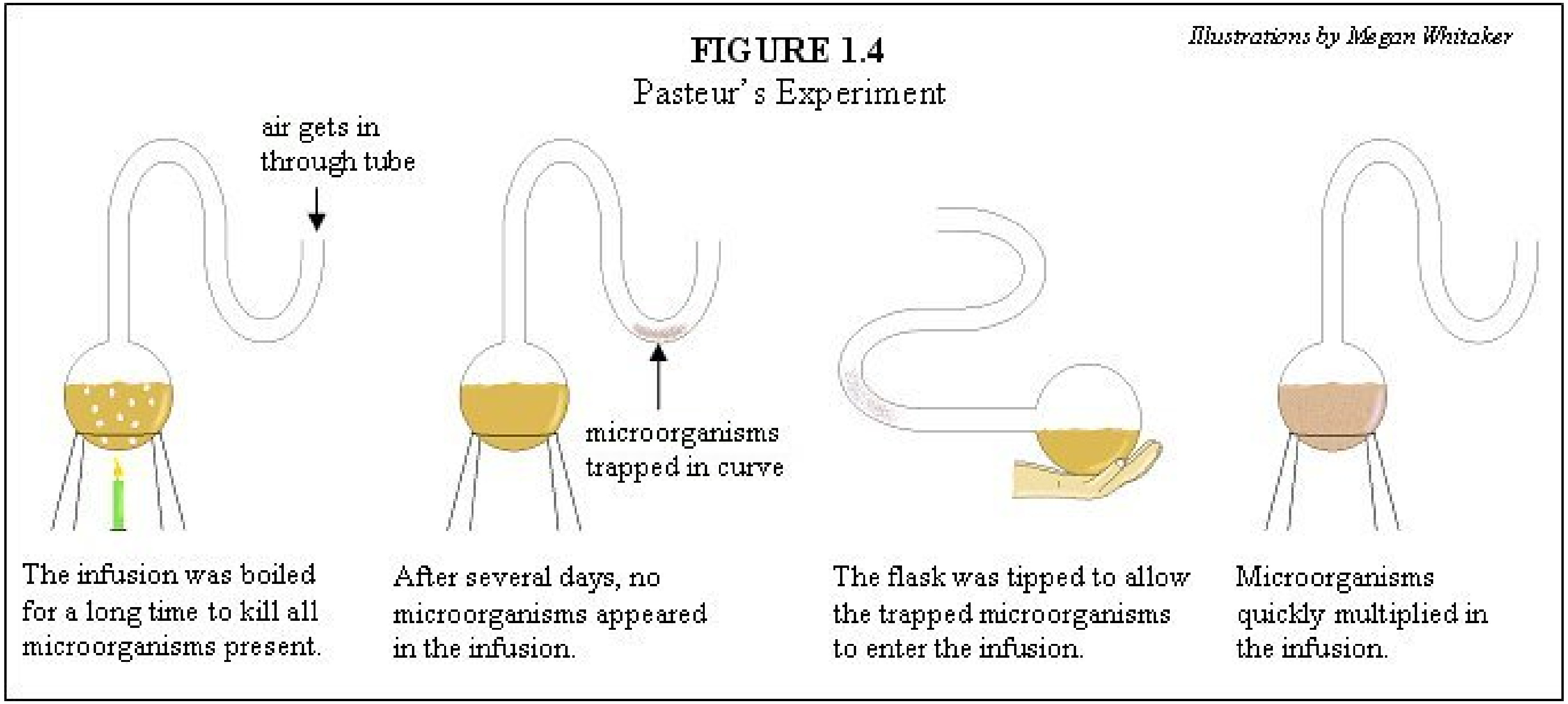
Louis Pasteur defied "vitalism", the spontaneous generation of life

1860s

Louis Pasteur
(1822-1895)
French chemist &
microbiologist

… until Louis Pasteur **disproved** the concept of "vitalism", the spontaneous generation of life via his **famous swan-neck bottle experiment**.

Key experiment by Louis Pasteur to defy "vitalism"(spontaneous generation): The famous swan neck flask experiment

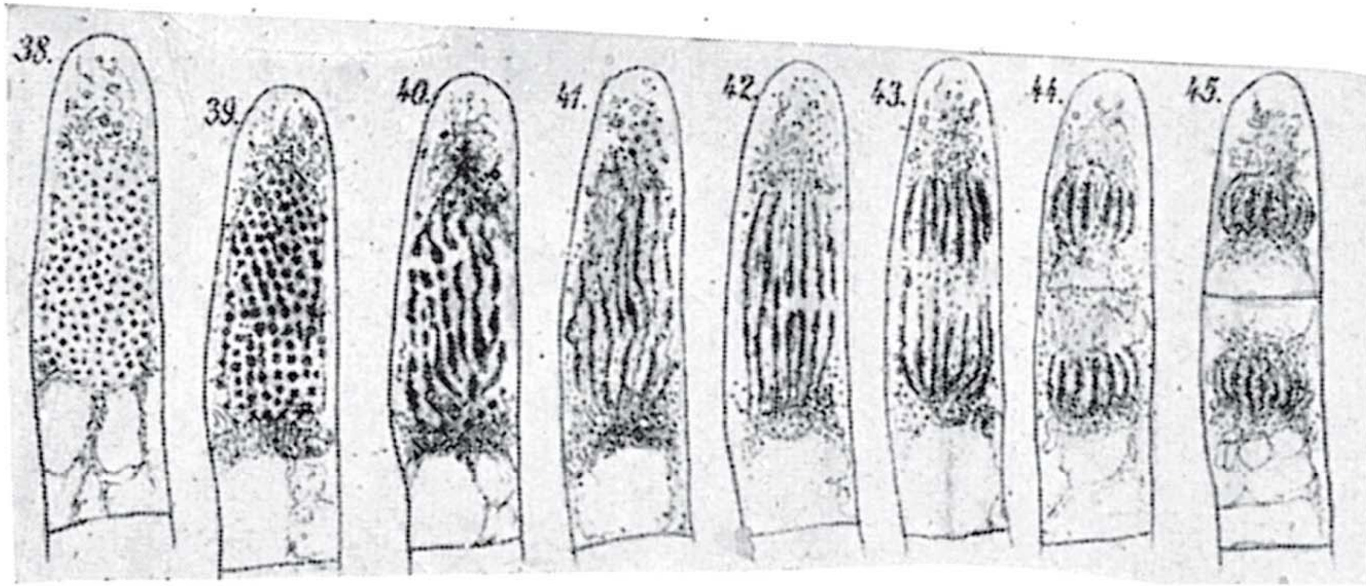


1.3 Cells only originate from a pre-existing living cell

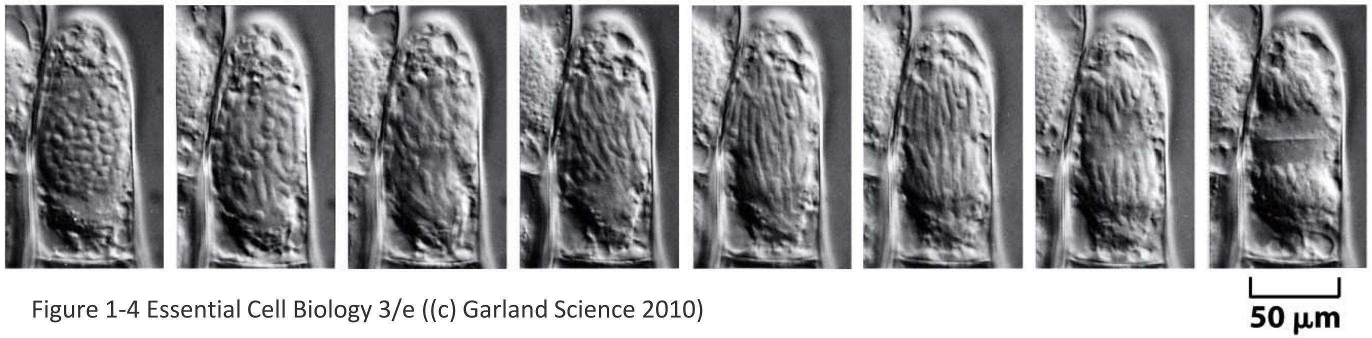
"**Never** will the doctrine of spontaneous generation **recover from the mortal blow** of this simple experiment."
"There is **no known circumstance** in which it can be confirmed that microscopic beings **came into the world without germs, without parents similar to themselves**."

Additional proof came from the observation of cell division

1880 Eduard Strasburger: cell division in hair cell from a *Tradescantia* flower



Original drawing (1880)

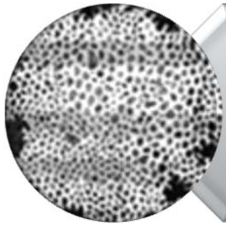


Light microscope (2010)

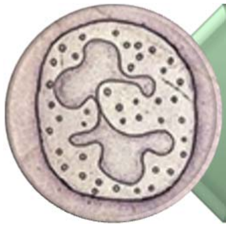
Figure 1-4 Essential Cell Biology 3/e ((c) Garland Science 2010)

The Cell Theory

The three tenets



1.All living organisms are composed of one or more cells



2.The cell is basic unit of structure and function for all organisms.

3.All cells arise only from preexisting cells by division.

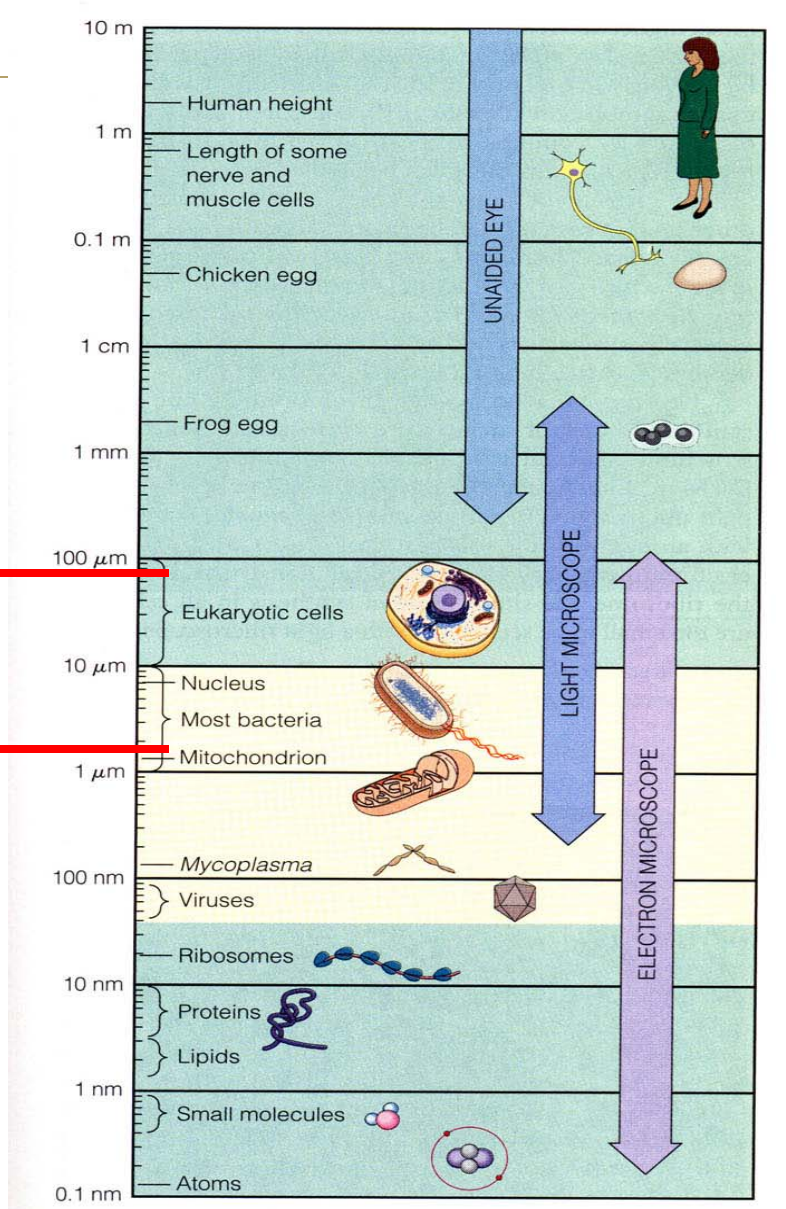
1.2 The differences between prokaryotic and eukaryotic cells

The size of cells varies greatly:

Most cells are small:

Prokaryotic: 1-10 µm

Eukaryotic: 10-100 µm



Size of bacteria, mammalian cells, yeasts?

The differences between prokaryotic and eukaryotic cells

The difference between a prokaryotic cell and an eukaryotic cell is the possession of a nucleus:

"eu" means "true", "good"

"karyote" means "kernel"

"pro" means "before"

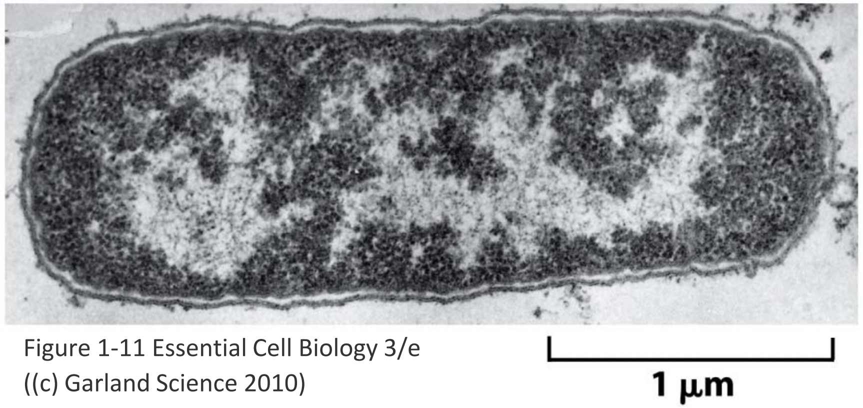


Figure 1-11 Essential Cell Biology 3/e
((c) Garland Science 2010)

Prokaryote:
Escherichia coli (*E. coli*)

Comparison between prokaryotic and eukaryotic cells

EUKARYOTIC Cells vs PROKARYOTIC Cells

CHARACTERISTIC	PROKARYOTES	EUKARYOTES
Size	0.2-2.0μm in diameter	10-100μm
Nucleus	x	ALL
Organelles with Phospholipid membrane	x	**ER, Golgi bodies, Lysosome mitochondrial, chloroplasts**
Glycocalyx	**capsule** (organize) **slime layer** (unorganize)	Surround some animal cells
Motility	*rotating* **Flagella** (some)	*undulated* Flagella & Cilia ("9+"2 arrangement microtubles others by *amboid action*
Flagella	some	some
Cilia	x	some
Fimbriae & Pili	some	x
Cell Wall	most, bacteria (peptidoglycan)	most: protein, cellulose, algin agar, carrageenan, silicate, glucomanna, chitin
Plasma membrane	Lacking carbs and sterols	has: glycoproteins, glycolipids, sterols
Cytosol	ALL	ALL
Inclusions	ALL	ALL
Endospores	some	x
Ribosomes	Cytoplasm (70s)	Cytoplasm (80s) Mitochondria & Chloroplast (70s)
Chromosomes	single, circular, lack **histones**	More than one, linear, contain **histones**
Cytoskeleton	**simple**	**complex**
Cell division	**amitosis**	**mitosis and meiosis**
Biochemical diversity	**much more**	**much less**

Structure and morphology of an eukaryotic animal cell

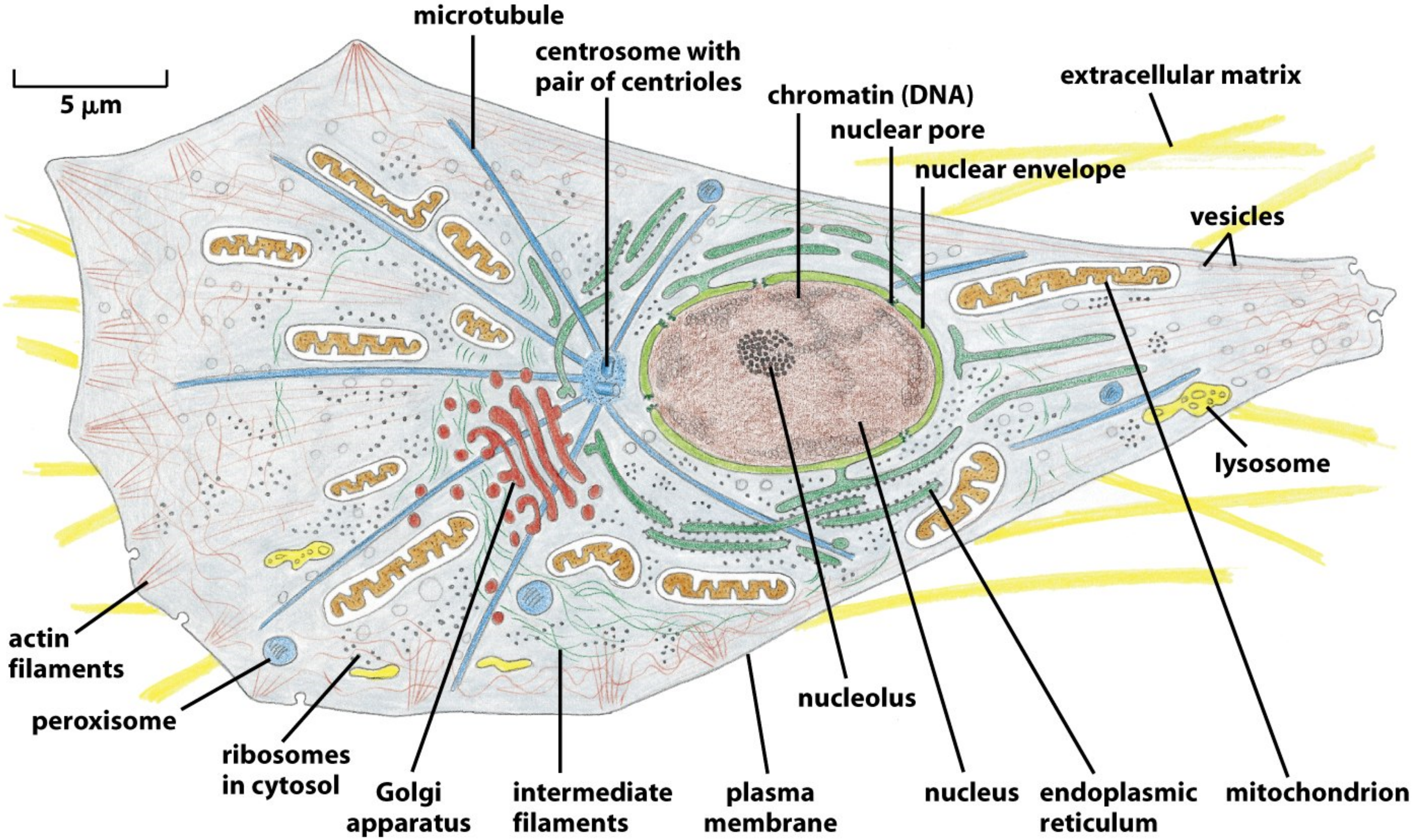
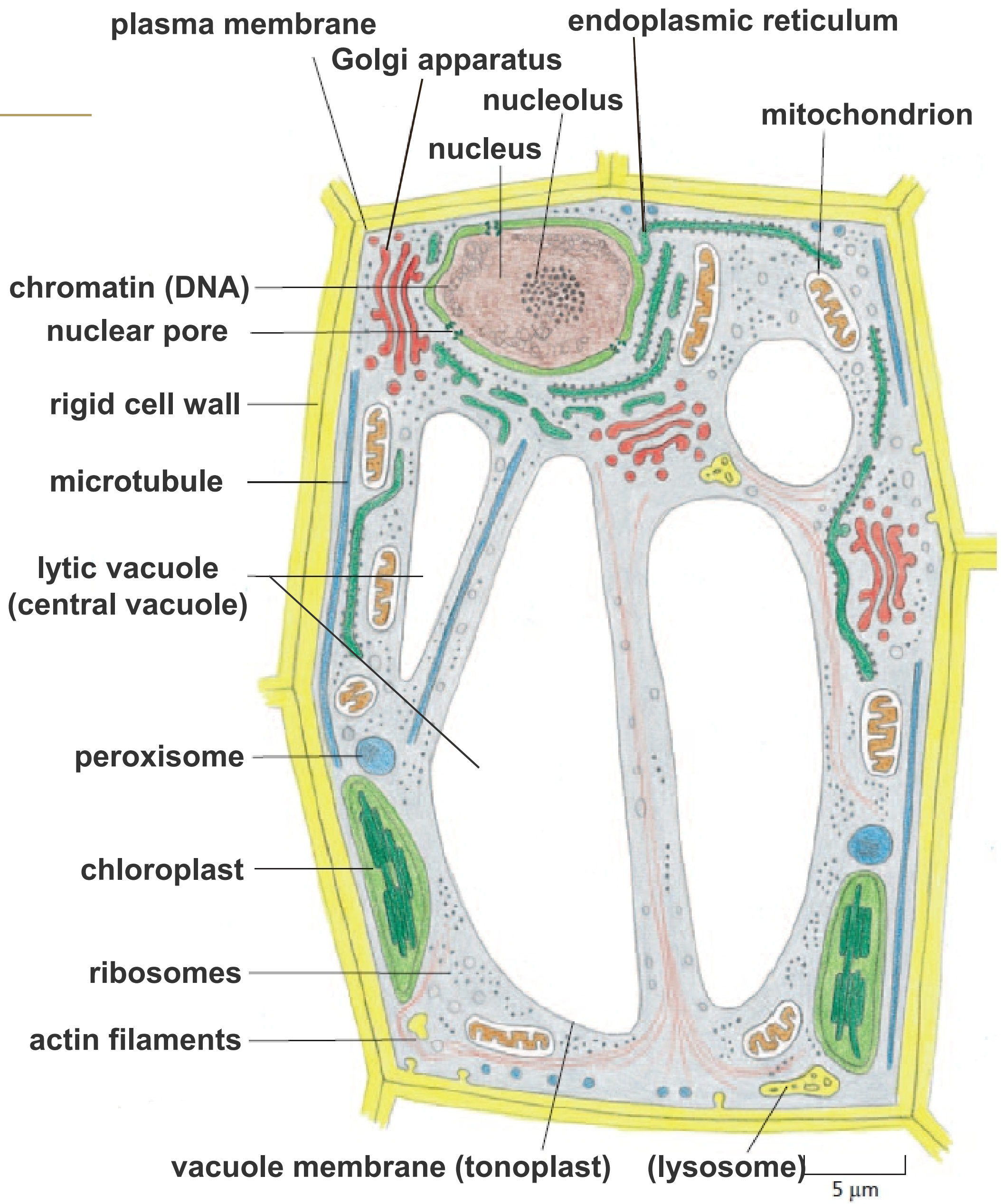


Figure 1-30 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Structure of a plant cell

Differences of plant cells compared to animal cells:

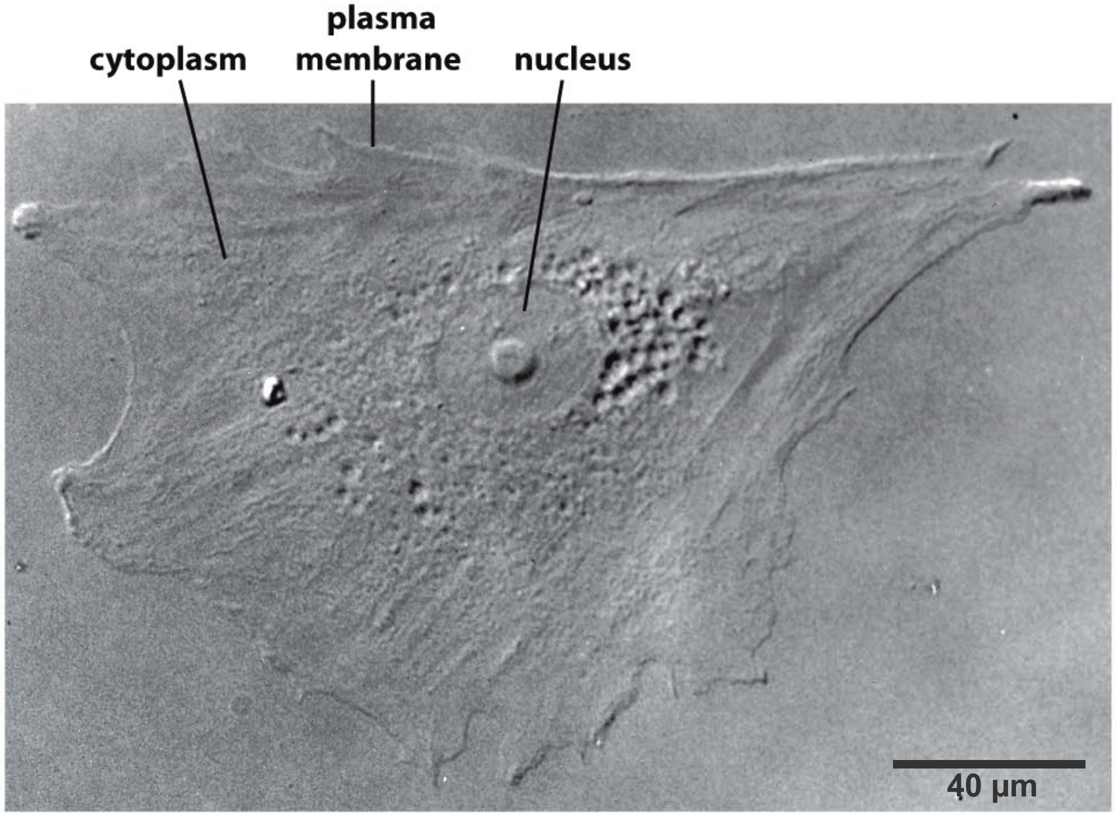
- rigid cell wall
- large central vacuole
- disperse Golgi stacks (dictyosomes)
- contain plastids:
  - Chloroplasts
  - Chromoplasts
  - Amyloplasts
  - Elaioplasts



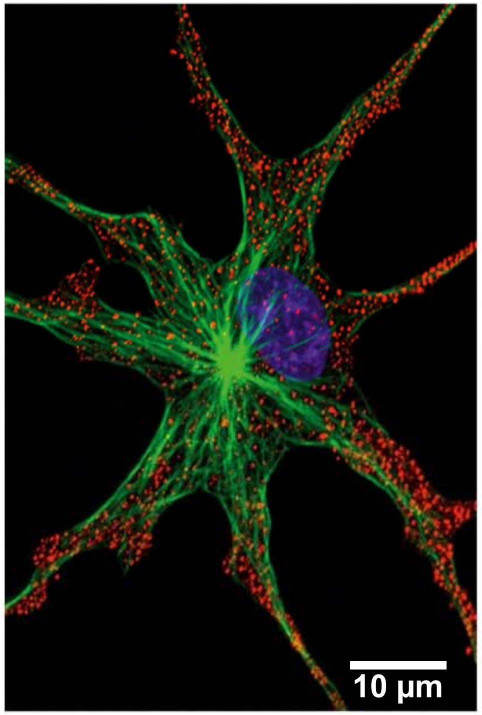
Cells visualized using microscopy: I) light microscopy

1) **Light microscopy**
(unstained)

2) **Fluorescence microscopy**
(stained/fluorescent dyes)



human skin cell

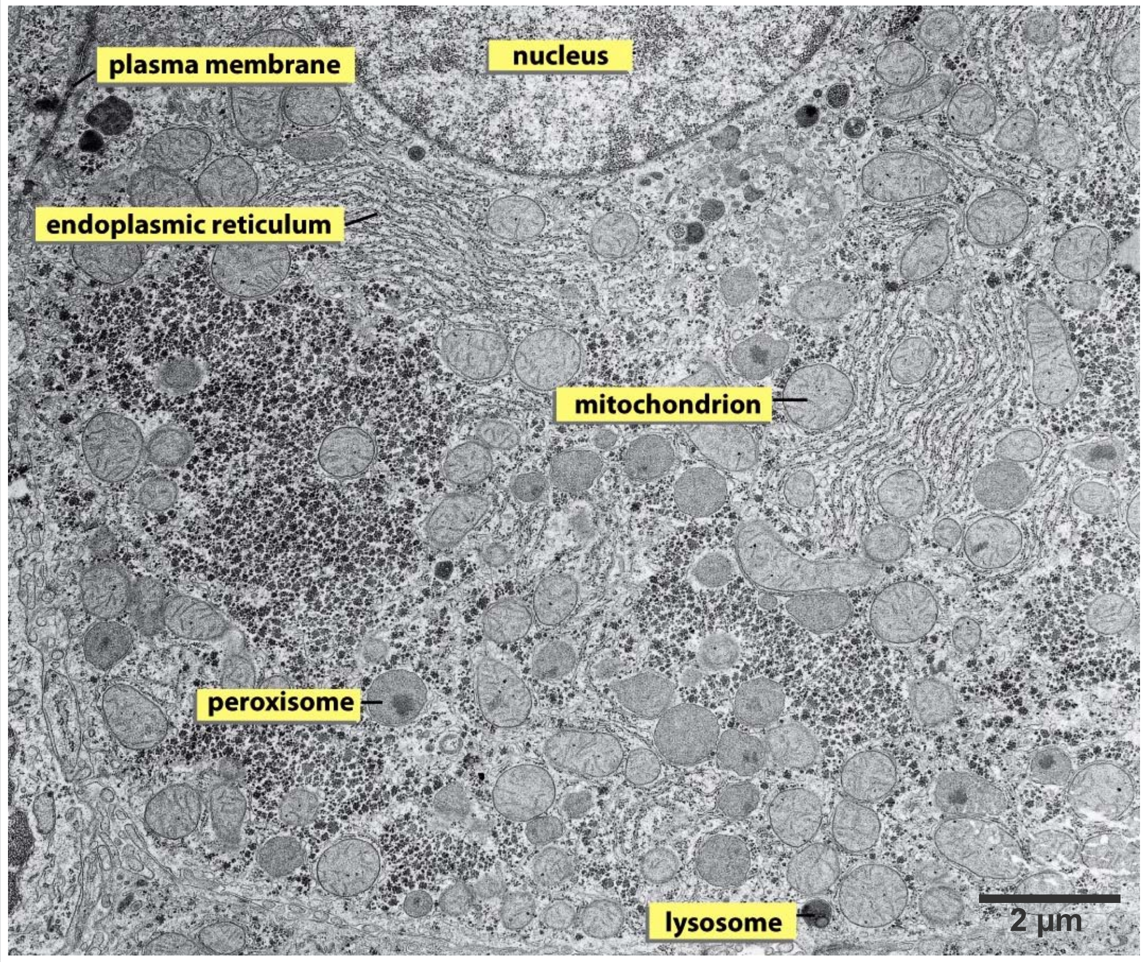


frog pigment cell

Remember: a fluorescence microscope is a light microscope: resolution **200nm**…

Cells visualized using microscopy: II) electron microscopy

3) Transmission electron microscopy (TEM)



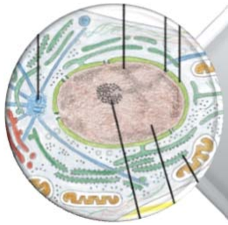
Electron microscopy reveals ultra structure of cells…

Figure 1-8a Essential Cell Biology 3/e (c) Garland Science 2010

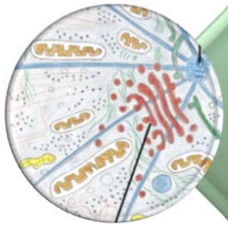
Remember: Resolution of an electron microscope: **50 picometer**…

Eukaryotes vs. prokaryotes

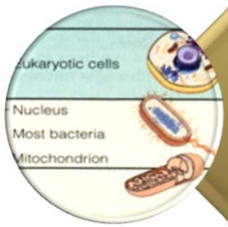
The three points to remember



1. Eukaryotes possess a “true” nucleus



2. Eukaryotes possess specialized intracellular compartments



3. Eukaryotic cells are usually larger than prokaryotic cells
(Size of a mitochondrion = size of prokaryote)

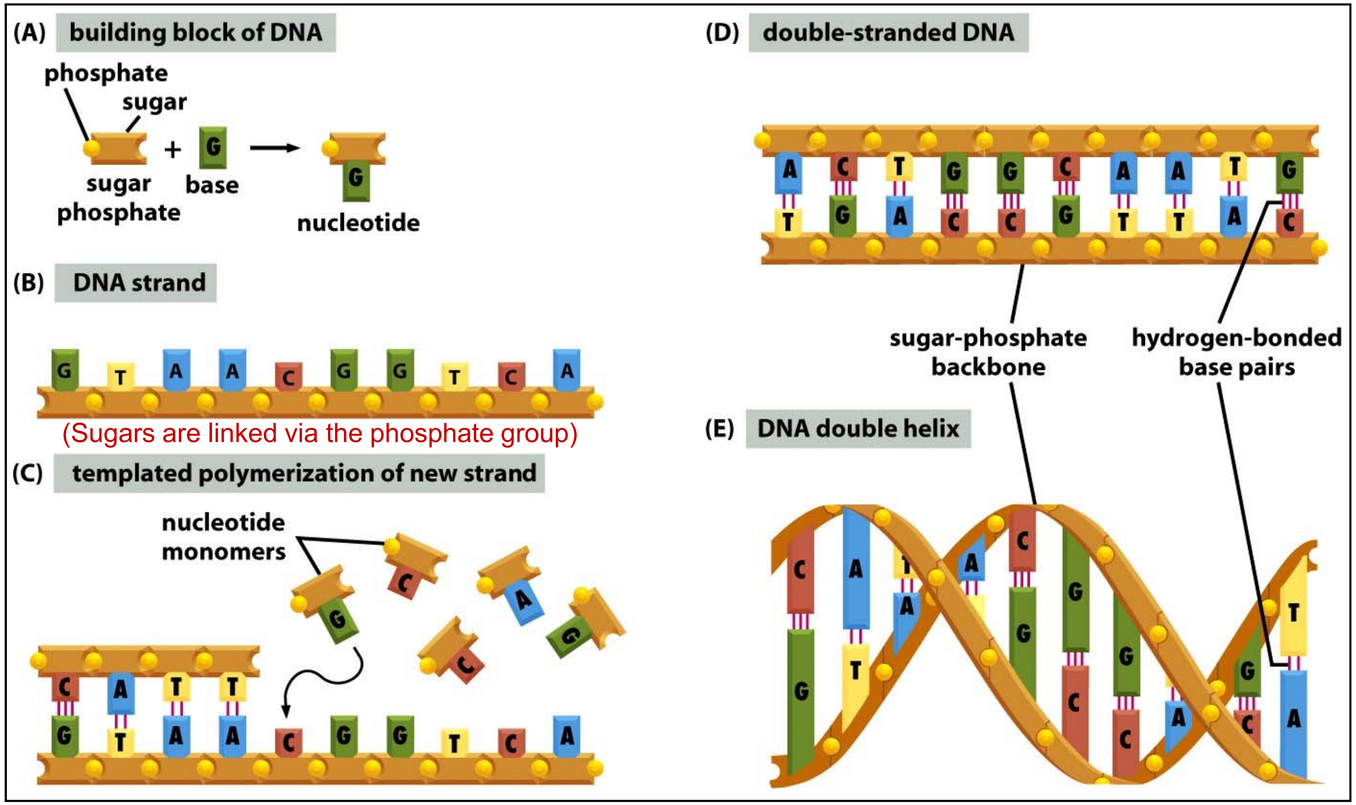
1.3 The astonishing constancy of all cells…

- Cells are much more complicated than any other
  known chemical system.
- Nothing in cells disobeys chemical and physical laws.
- All cells are composed of small molecules,
  from which large polymers are assembled
  to execute the cell function, but with remarkable constancy.

How is this achieved?

Hereditary information is stored in DNA (desoxyribonucleic acid)

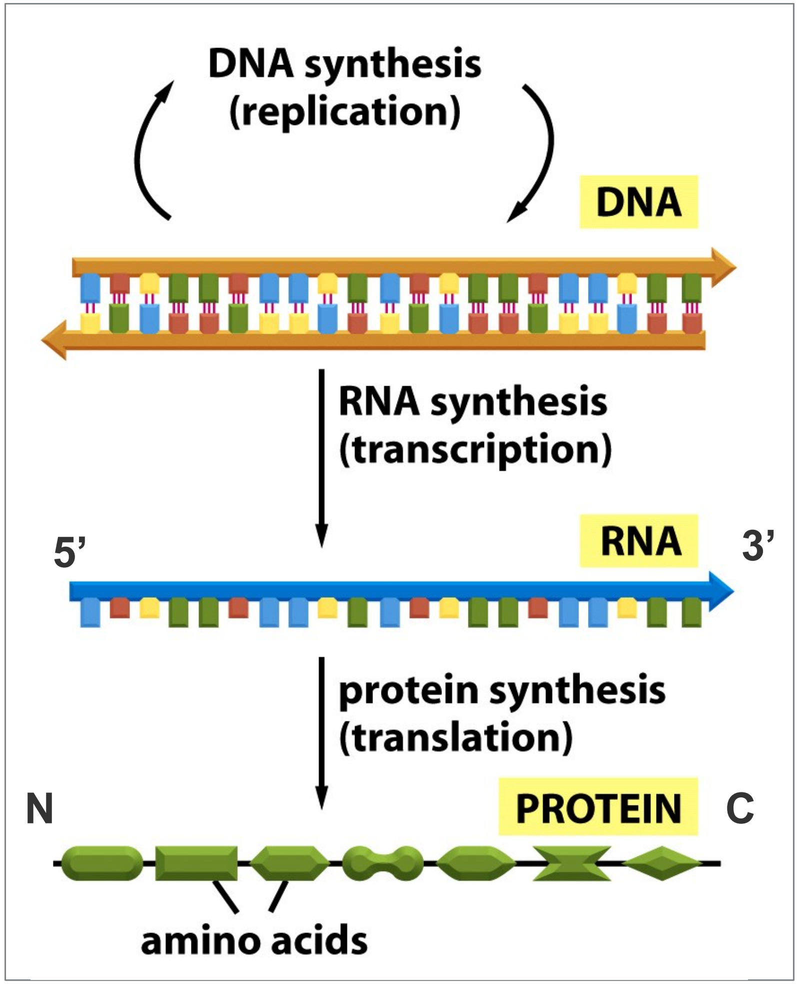
1) All cells use DNA to store hereditary information.
   Information is passed on by DNA replication, the templated polymerization



All cells use the same set of 4 bases in DNA: A (adenine), G (guanine), C (cytosine), T (thymine)

Genetic information is stored in DNA and translated in to protein

2) All cells transcribe DNA into RNA, and translates RNA into protein, which has various functions in cells

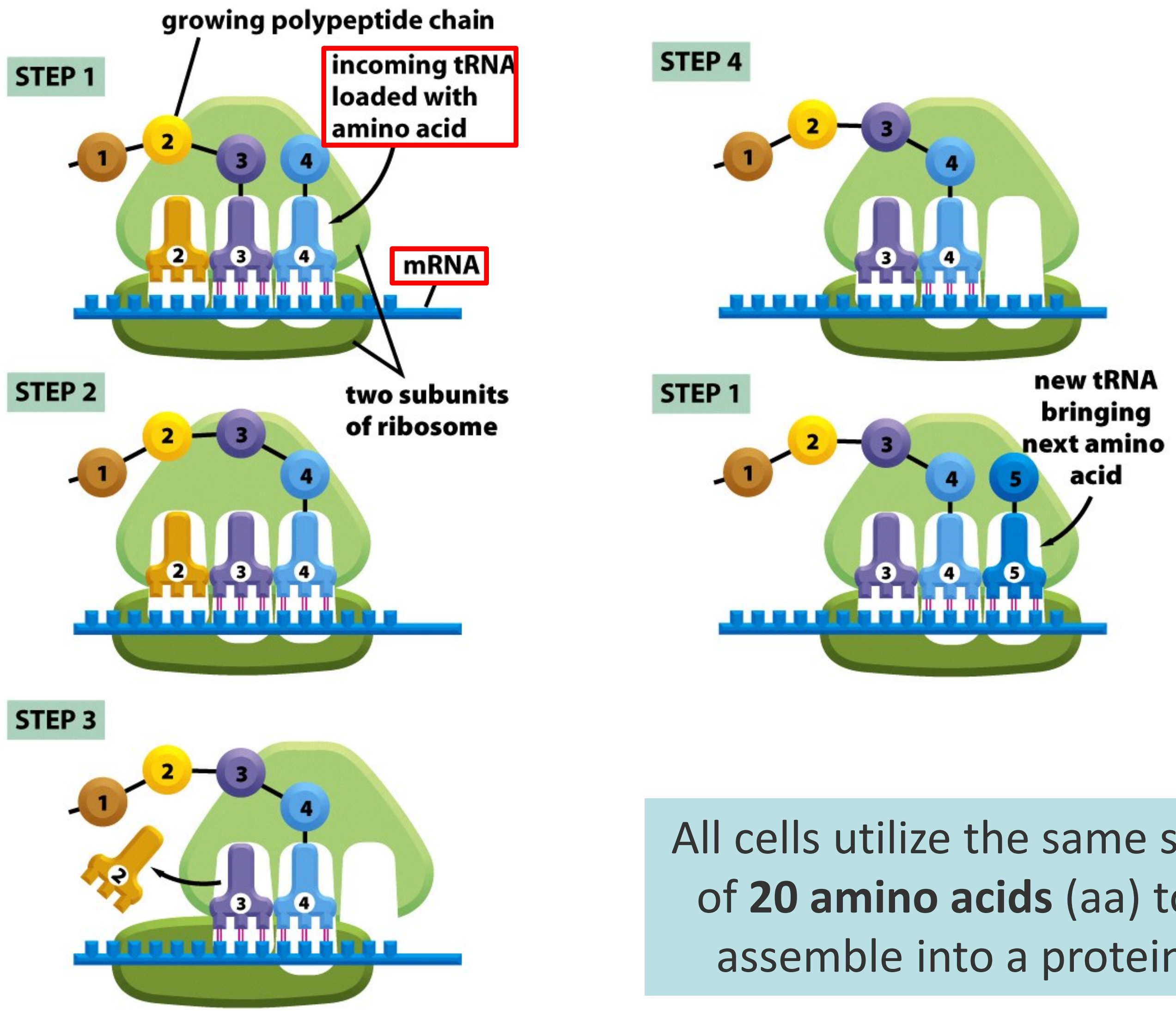


DNA (**deoxy**ribonucleic acid)
- usually double-stranded
- bases used:
  adenine, guanine, cytosine & **thymine**

RNA (**ribo**nucleic acid)
- usually single-stranded
- bases used:
  adenine, guanine, cytosine & **uracil**

Two-step procedure:
1) Transcription into RNA
2) Translation into protein

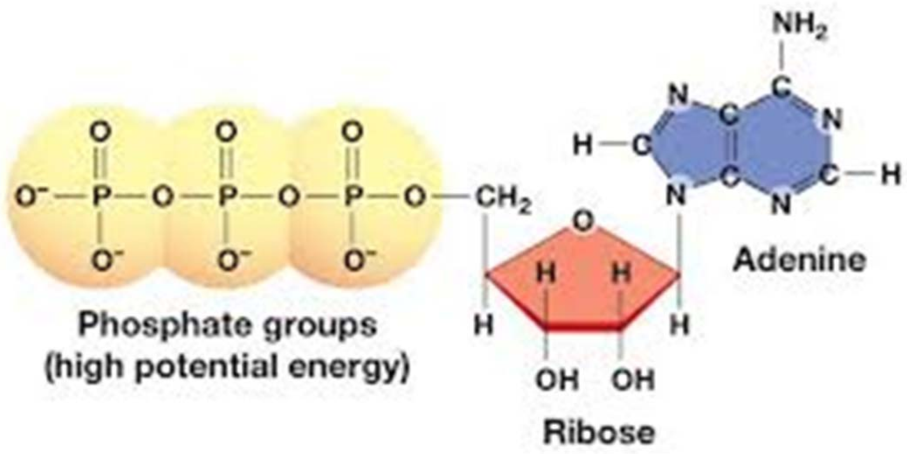
Protein synthesis from messenger RNA by ribosomes



All cells utilize the same set of **20 amino acids** (aa) to assemble into a protein

The universal energy carrier ATP (adenosine triphosphate)

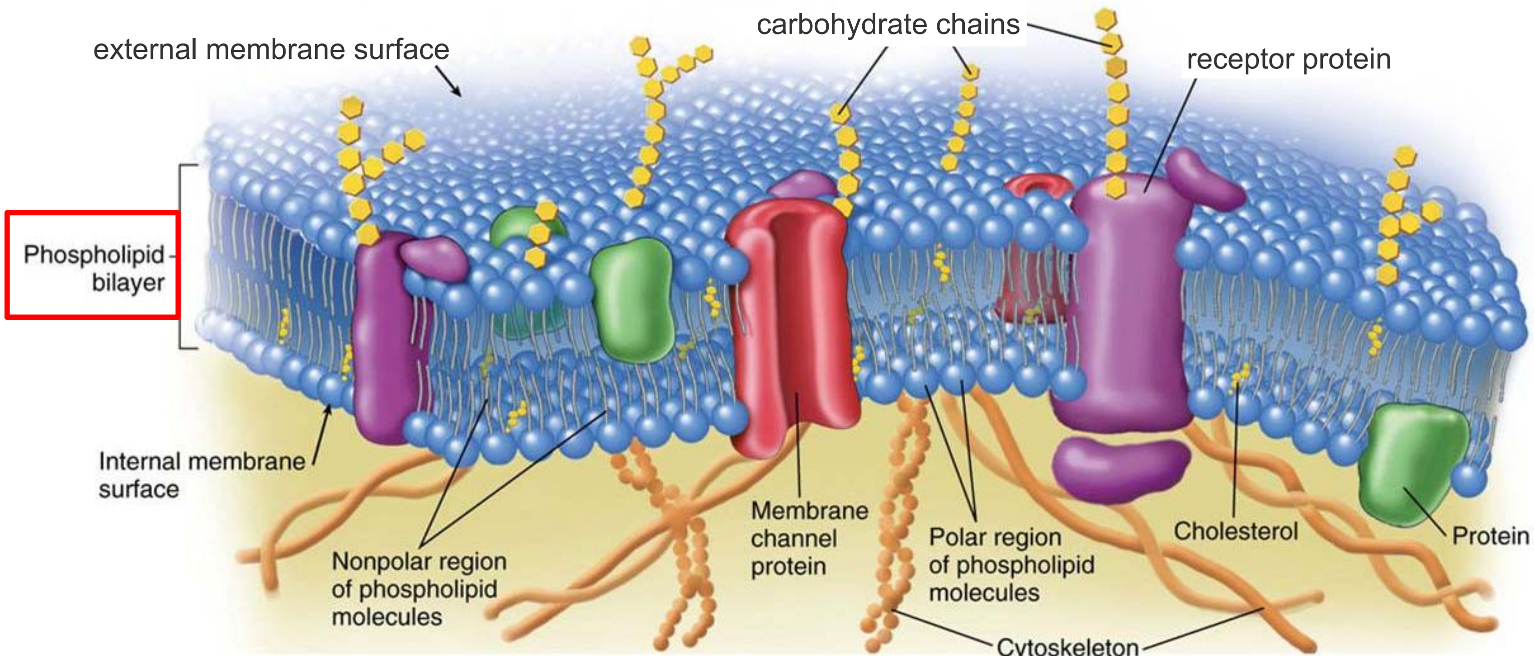
3) All cells require free energy and all cells make and consume ATP to drive cellular activities



Cells are highly ordered, to maintain the order, they have to consume energy

Separation of the cellular content from the exterior

4) All cells are enclosed in a plasma membrane

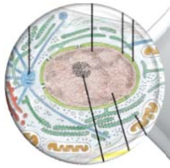


Functions of the plasma membrane:

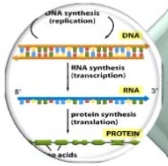
1. Maintain its integrity as a coordinated chemical system
2. Retain the nutrients and useful products for its use
3. Excreting waste products
4. Membrane-embedded proteins as signaling molecules, sensing outside stimuli

Constancy of cells

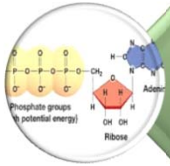
The four points to remember



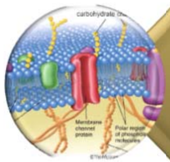
1. Genetic information is stored in DNA



2. DNA is transcribed in RNA and is translated to protein



3. The universal energy form is ATP



4. The plasma membrane separates the cellular content from the exterior

1.4 How did cells evolve?

All living organisms consists out of cells, derived from a common ancestor

Diversity of lives on earth

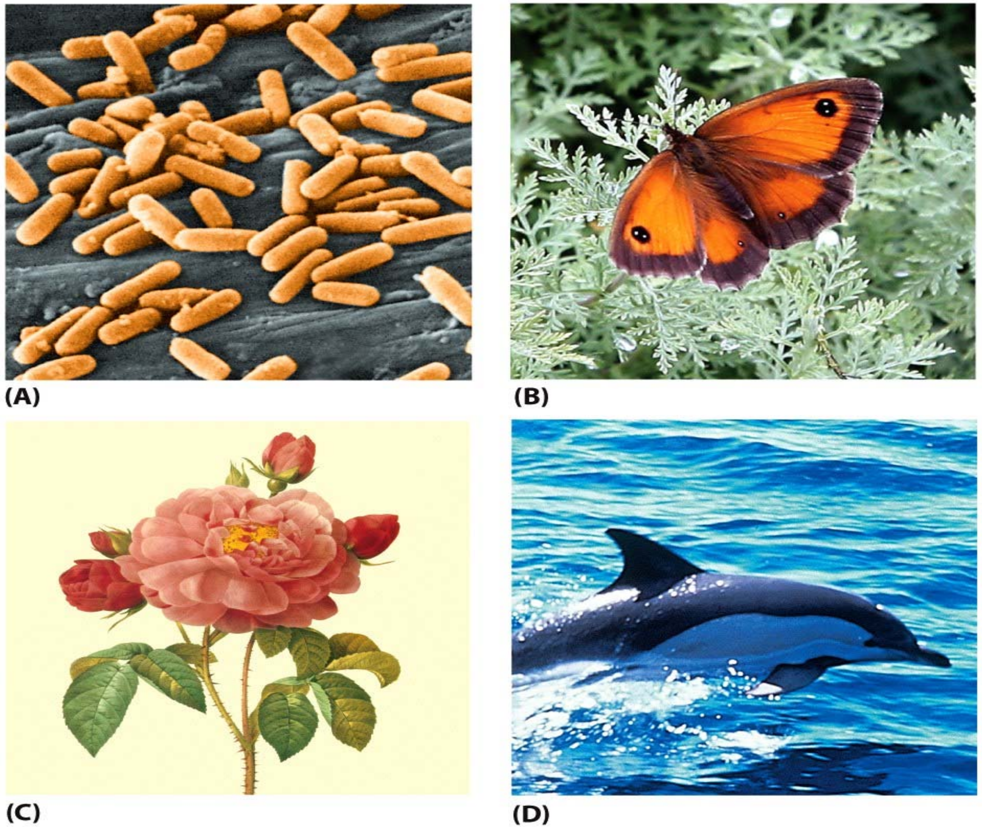


Figure 1-3 Essential Cell Biology 3/e (© Garland Science 2010)

Timeline for Evolution of Life on Earth (from Fossil record)

Time line (years ago)	Event
4600 million	The planet earth forms
3900-2500 million	Cells resembling prokaryotes appear
3500 million	Split between bacteria and archaea occurs
2700 million	Cyanobacteria evolve
1850 million	Unicellular eukaryotic cell appear
1200 million	Simple multicellular organisms evolve
580-500 million	Most modern phyla of animals begin to appear
485 million	First vertebrates with true bones evolve
434 million	First primitive plants arise on land
225 million	Earliest dinosaurs appear
215 million	First mammal evolve
65.5 million	Extinction of dinosaurs and almost half of all animal species
6.5 million	First hominids evolve
2 million	First members of the genus Homo appear
200 thousand	Anatomically modern humans appear in Africa

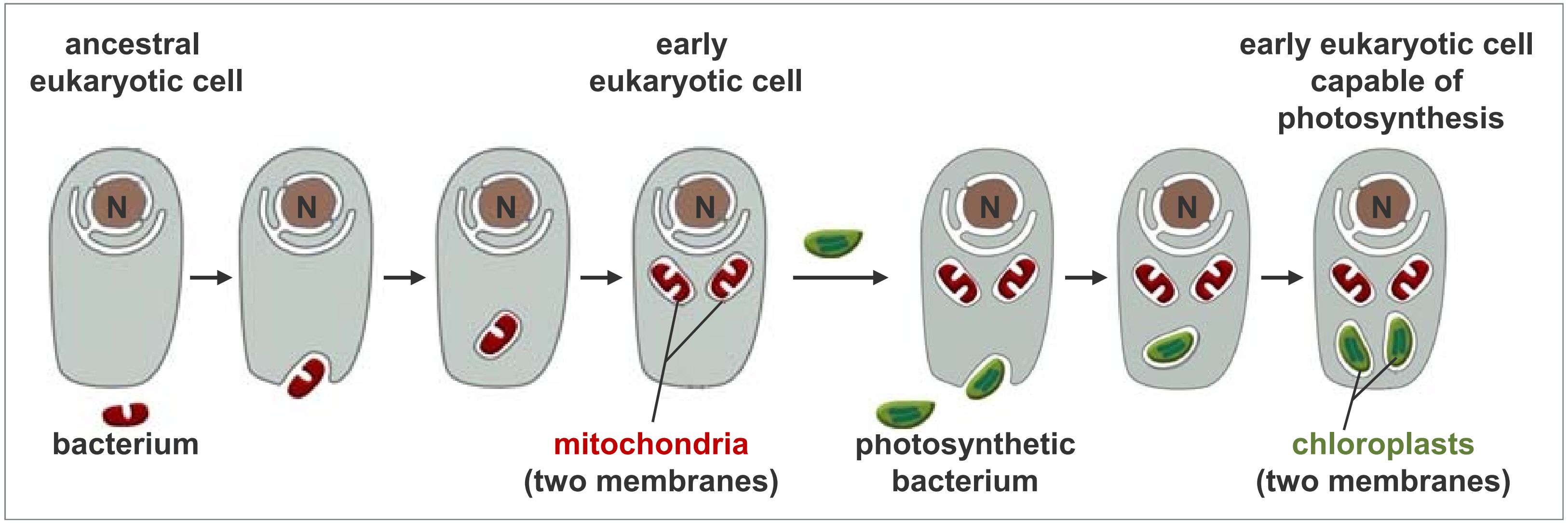
---adapted from *Molecular Cell Biology*, 7th edition

How does an eukaryote evolve?

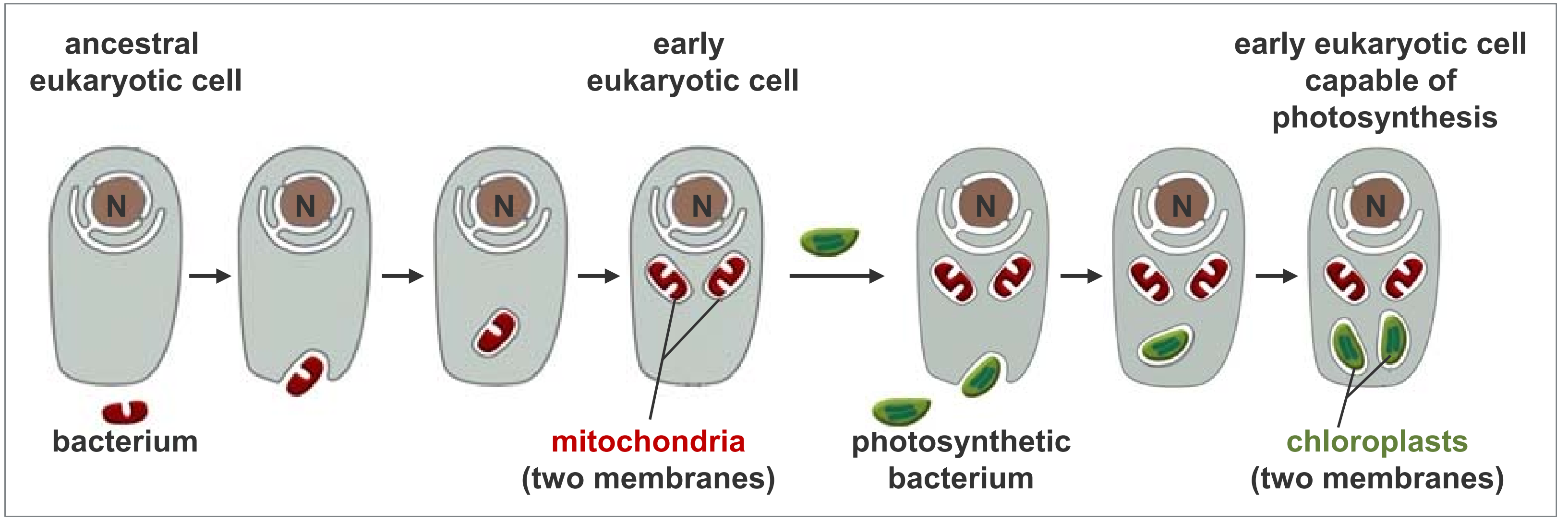
It is a mystery how the primordial eukaryotic cell evolved!

Hypothesis:

Ancient eukaryote might have been a predator, mitochondria and chloroplasts might be the result of engulfing of oxygen-metabolizing bacteria and photosynthesis bacteria, respectively (**endosymbiosis hypothesis**)



Evidence to support symbiosis



- Mitochondria and chloroplast are the **size** of a bacterium
- Mitochondria and chloroplasts have **two** different membranes
- Some **different** genetic codons are utilized to encode proteins
- Mitochondria and chloroplast have their separate but cut-down versions of **genomic DNA**, **ribosomes**, **tRNA**, that resemble those of bacteria.

… only mitochondria and plastids possess two membranes, all other compartments possess only one membrane ….

Genetic information determines the nature of whole multicellular organisms

The fertilized egg cell contains all required information…

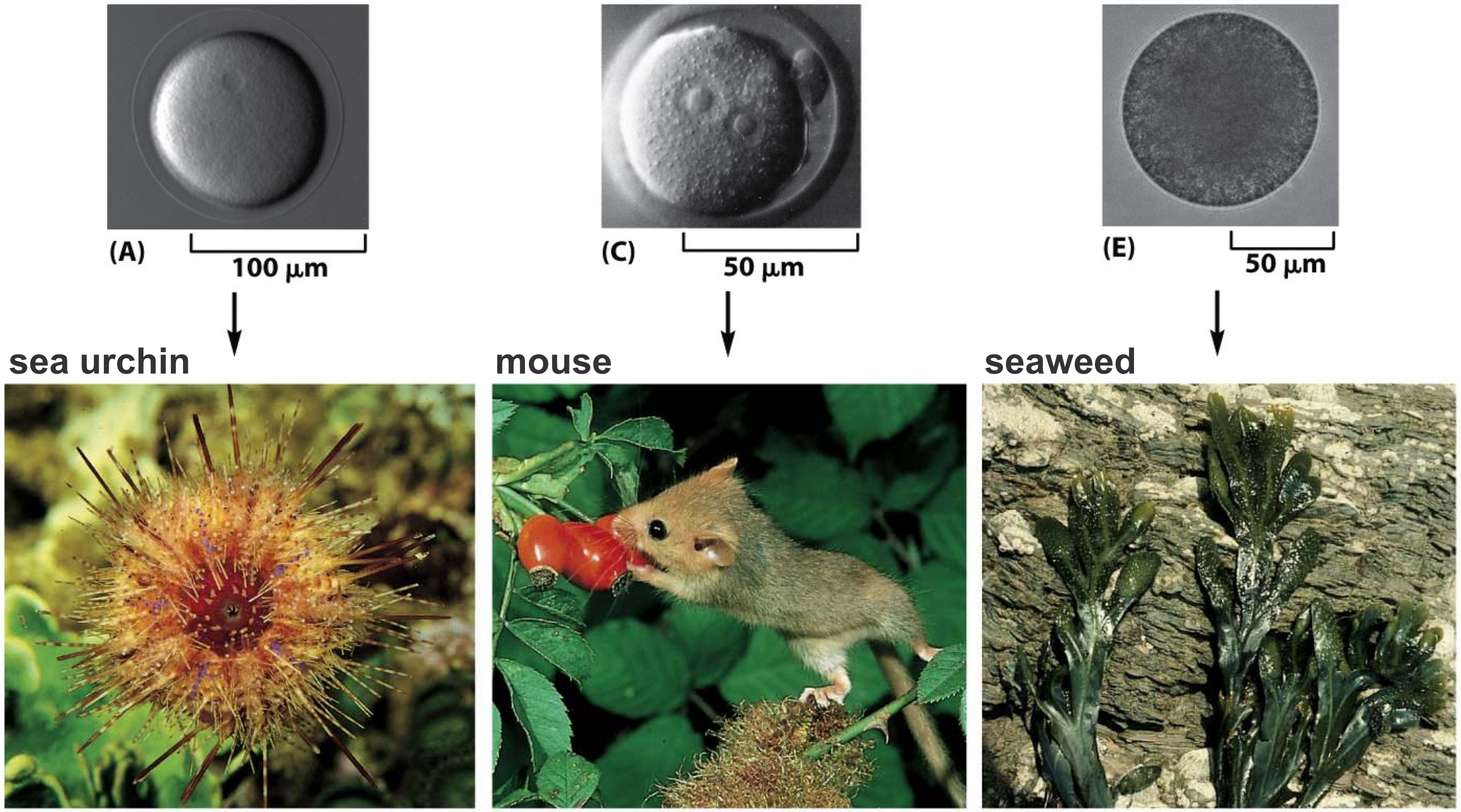
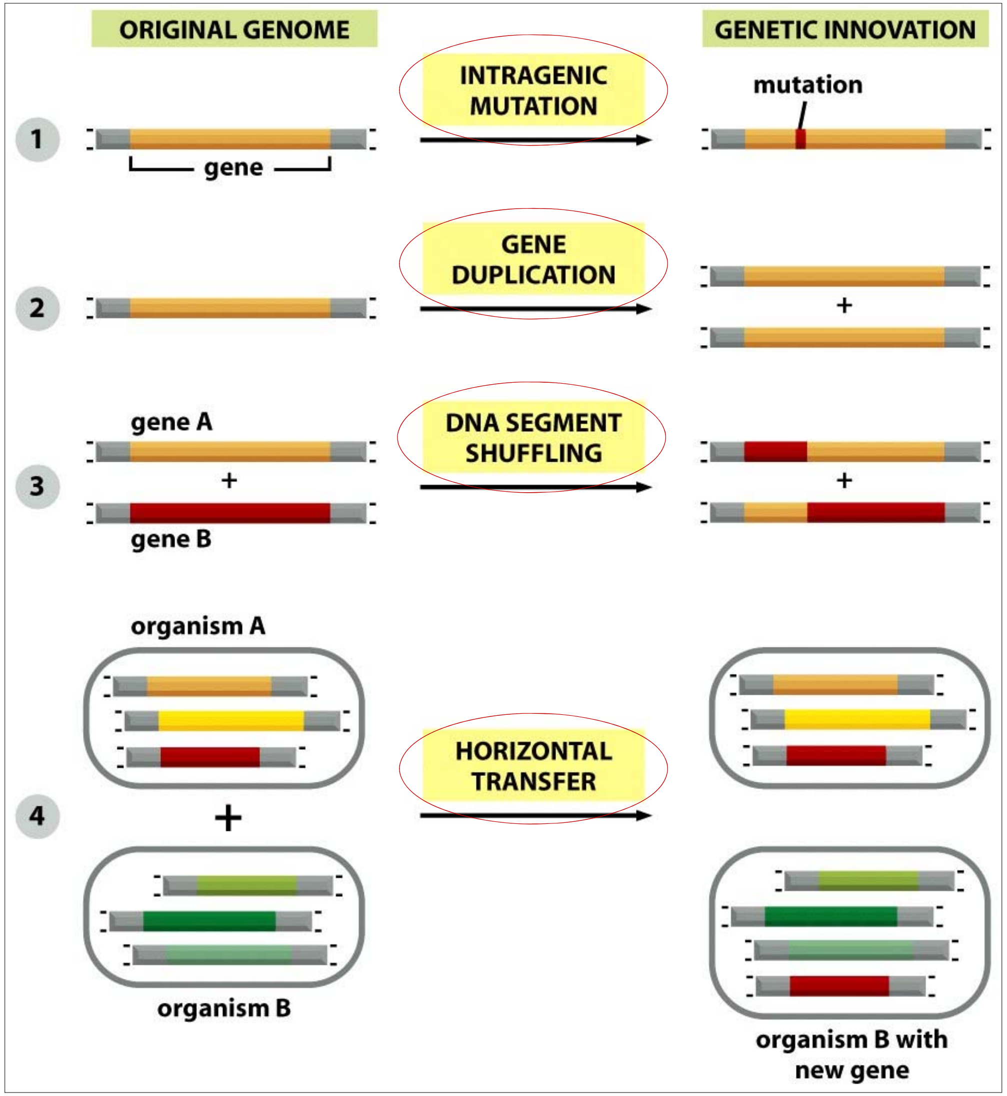


Figure 1-1 Molecular Biology of the Cell (c) Garland Science 2010

Species evolve from prokaryotic to eukaryotic, from single cell to multicellular cell, the genome size and gene all increase, how do they expand their genes?

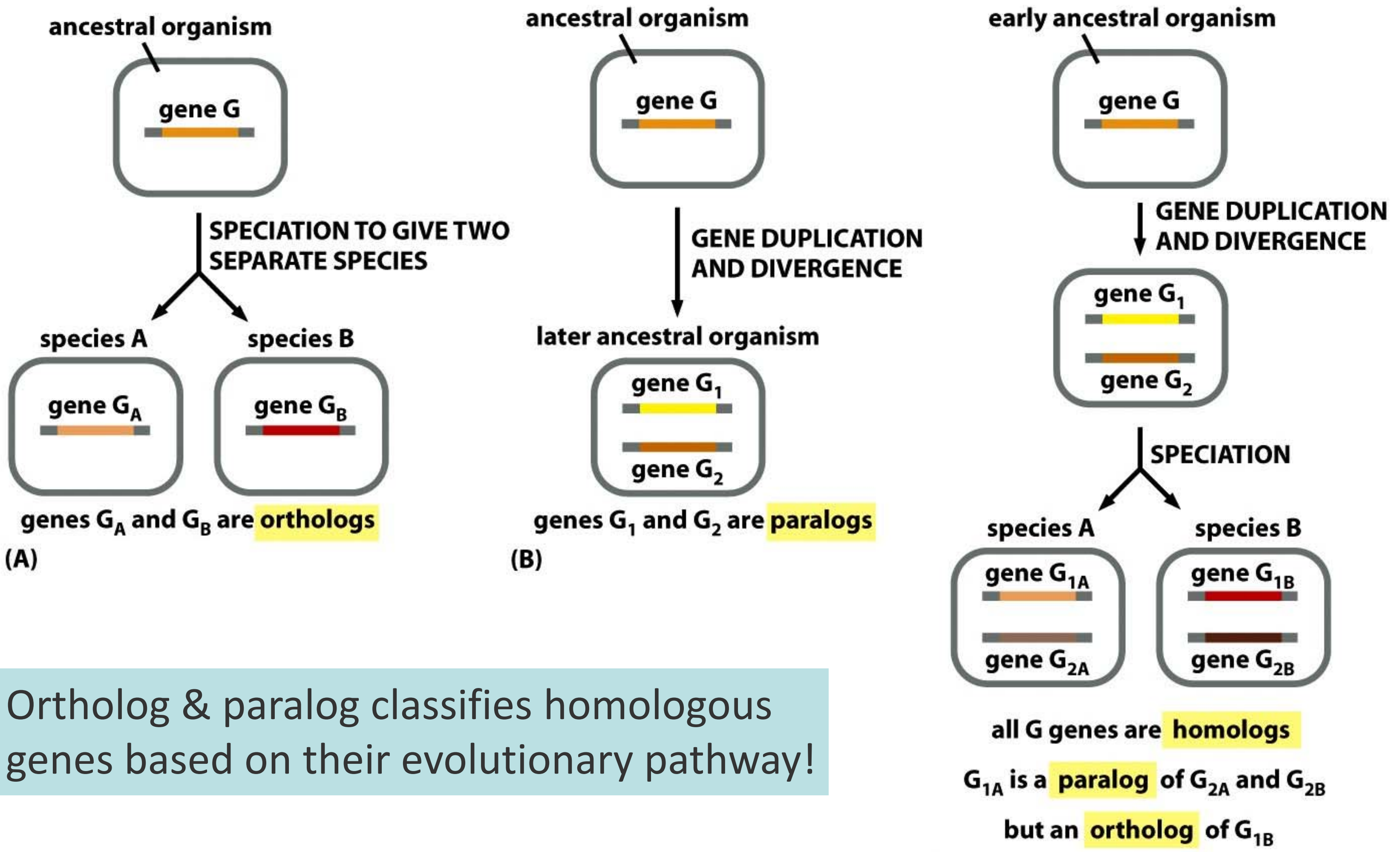


Four ways of innovation:

1. Mutations
2. Duplications
3. Shuffling
4. Horizontal gene transfer (versus vertical transfer from parent to progeny)

New genes are generated from preexisting genes…

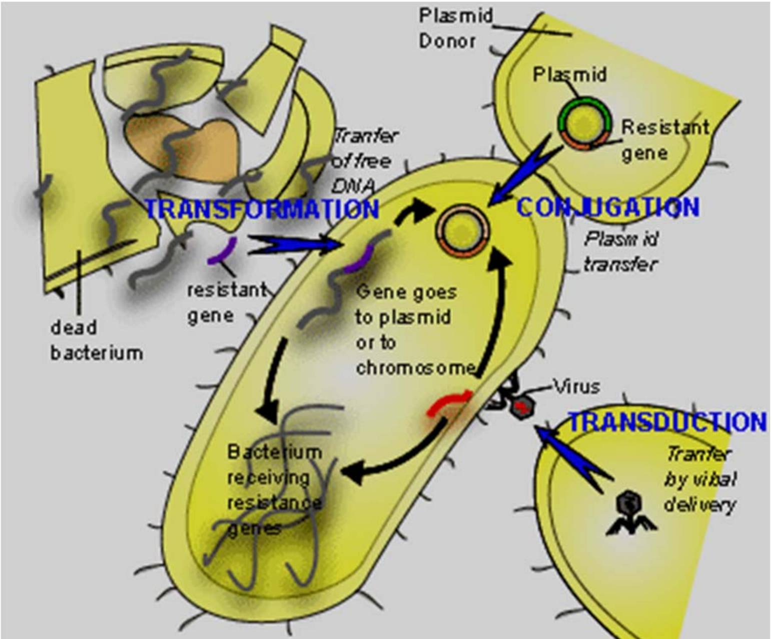
Different evolutionary pathways yield homologous genes:



Ortholog & paralog classifies homologous genes based on their evolutionary pathway!

Horizontal gene transfer (HGT)

HGT occurs in prokaryotic cells within the same species or between species



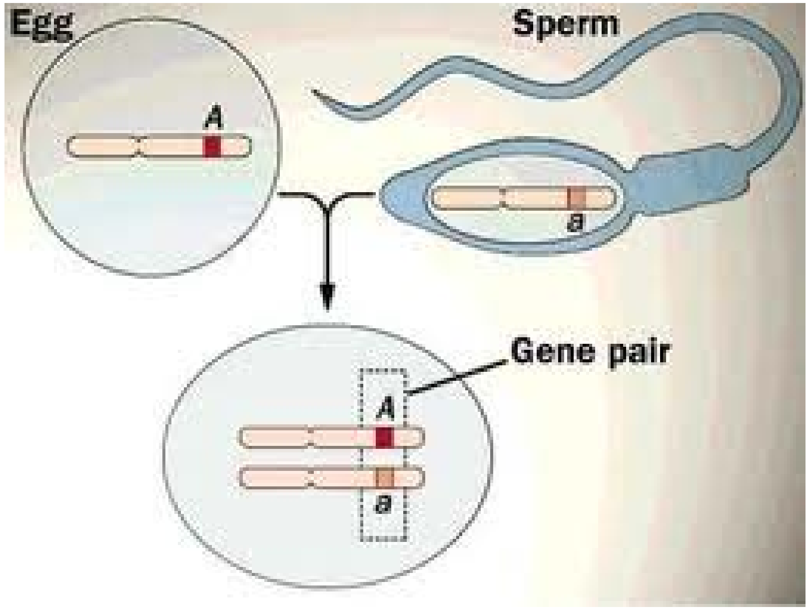
http://news.ifeng.com/a/20170515/51091274_0.shtml

Three ways of horizontal gene transfer:

- Transformation
  (transfer/uptake of free DNA)
- Conjugation
  (Cell to cell transfer of plasmid DNA)
- Transduction
  (Transfer by viral delivery)

Horizontal gene transfer (HGT)

Horizontal gene transfer in higher organisms, by sex

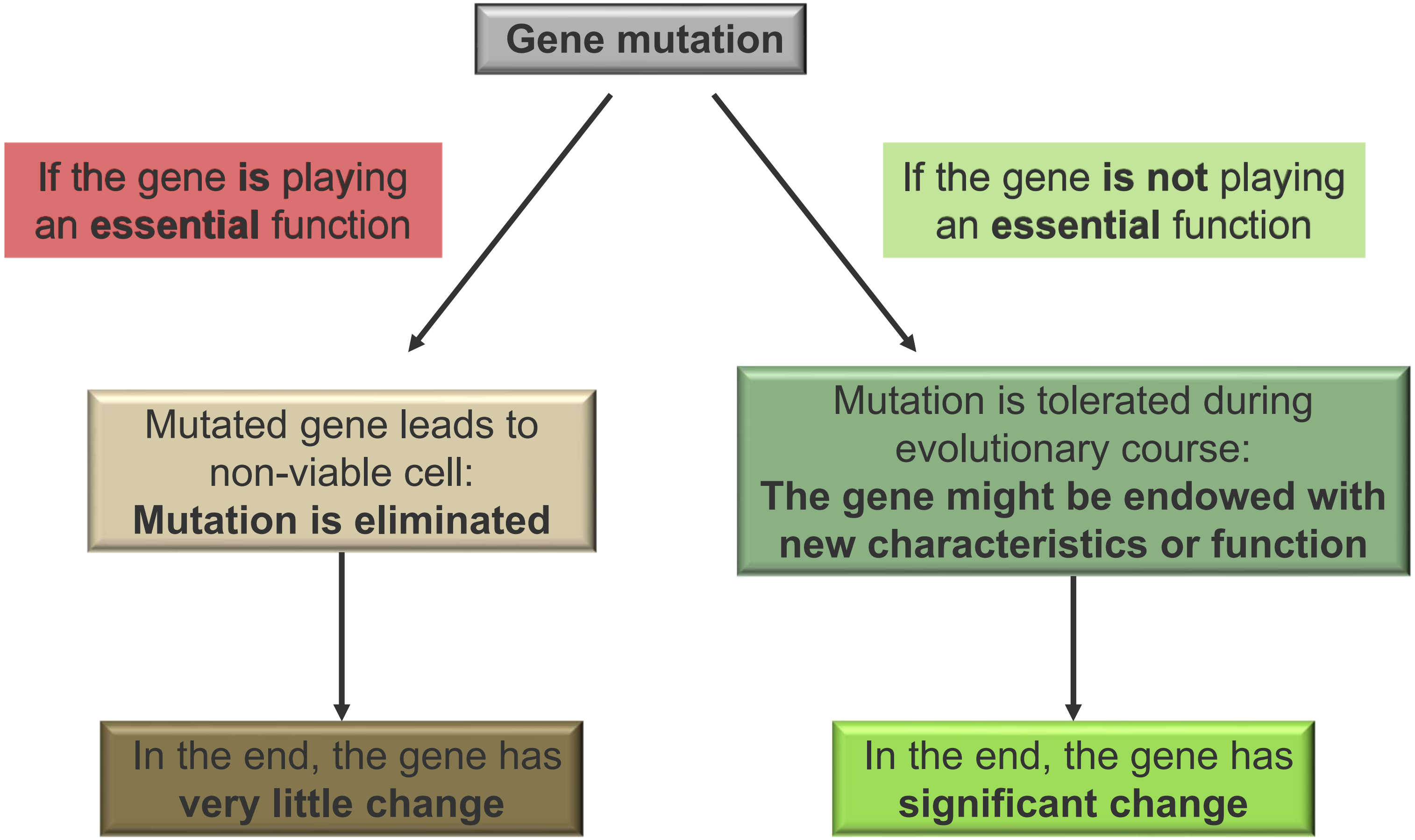


Horizontal gene transfer in higher organisms:

- Fusion of sperm cell & egg cell (sexual reproduction)
- HGT also occurs in human via virus infection

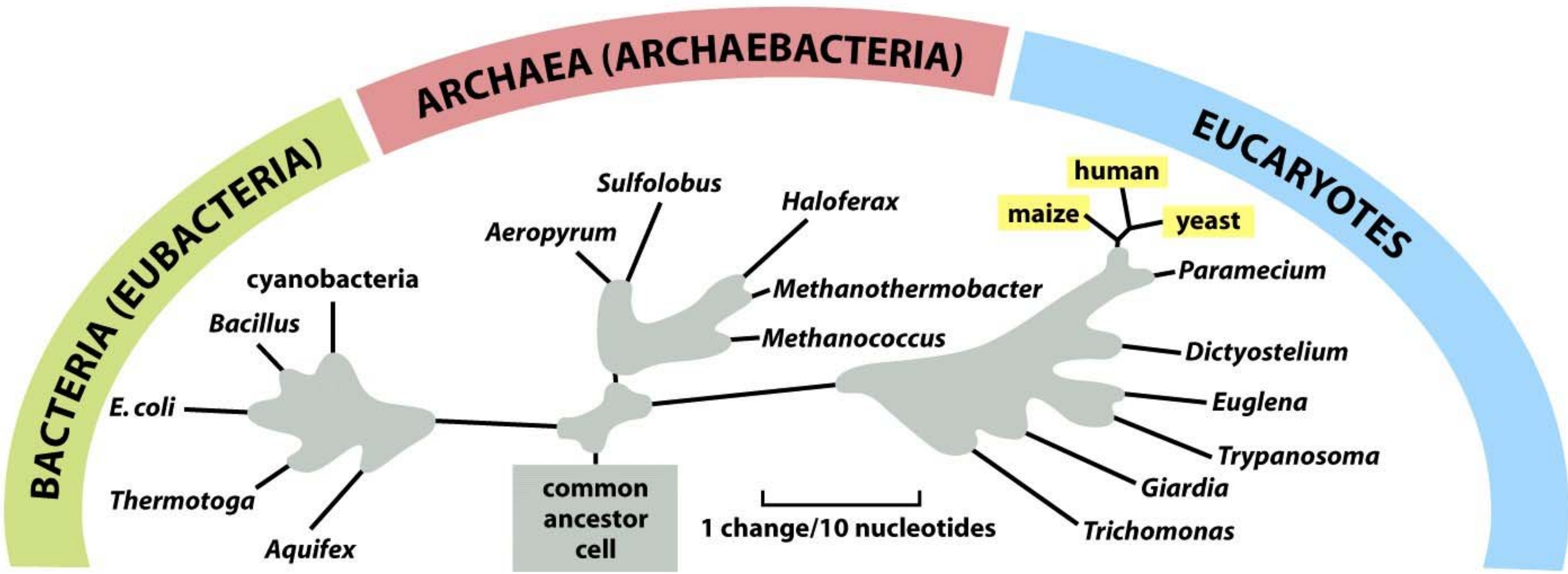
Why are some genes evolve rapidly, while others not?

Random mutation of DNA occurs during DNA replication :
for the better or the worse…



Genetic sequence allows simpler and more accurate way to determine evolutionary relationship, based on essential genes

Phylogenetic tree of life by ribosomal RNA (rRNA) sequencing



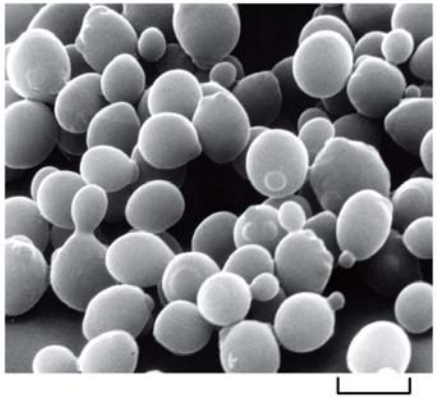
Archaea resemble eukaryotes in DNA replication, transcription and translation but resemble eubacteria in metabolism and energy conversion.

1.5 The application of model systems to study cell biology

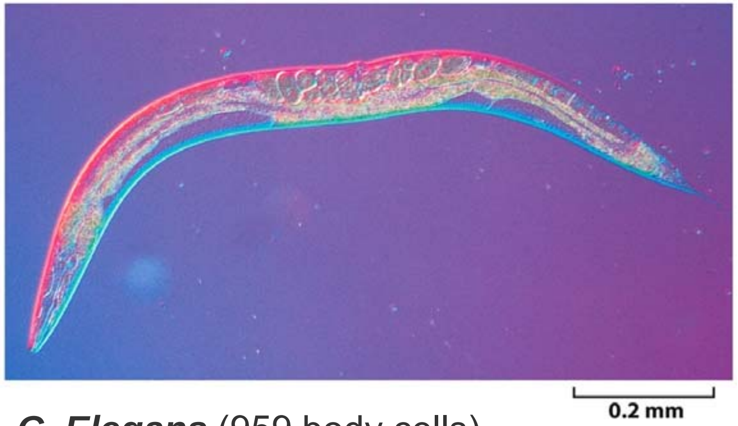
Considerations for choosing a model system:

- Size of the genome
  (the smaller the better)
- Short life cycle
- Easy manipulation
- Costs of the system
  (the cheaper the better)
- Ethical considerations
- Mutations available

Commonly used model systems

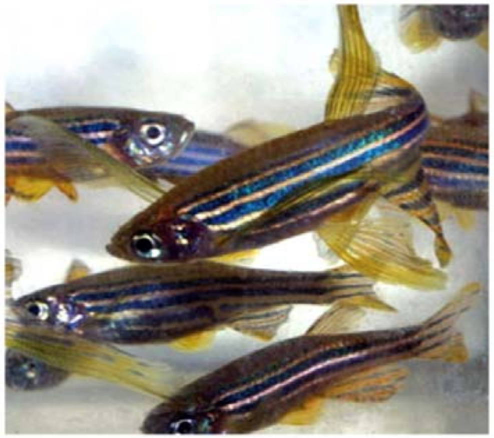


S. cerevisiae



C. Elegans (959 body cells)

Arabidopsis thaliana
(small genome,
offsprings after 10 weeks)



Zebrafish
(easy to grow vertebrate,
transparent larvae)

Drosophila melanogaster
(large chromosomes,
little gene duplications)

Mouse

Model systems that have been fully sequenced

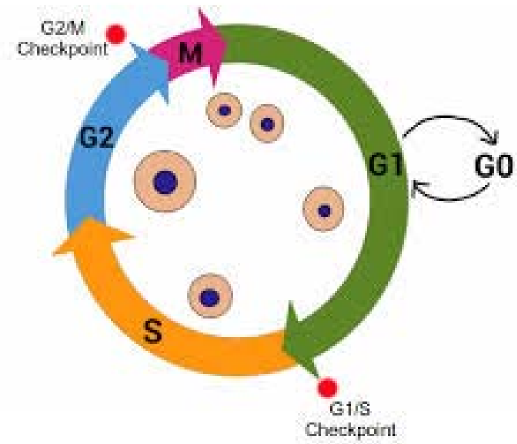
	Base pairs (millions)	encoded protein	chromosomes
• Bacteria (*E. coli*)	4.64	4289	1
• Yeast (*S. cerevisiae*)	12.16	5885	16
• Worm *(C. elegans)*	100	20424	6
• Fruit fly(*D. melanogaster*)	168	13781	4
• Zebrafish (*Danio rerio*)	1505	19929	25
• Mice(*Mus musculus*)	3421	22085	20
• *Arabidopsis thaliana*	135	27416	5
• Human (*Homo sapiens*)	3279	21077	23

—— **Adapted from *Molecular Cell Biology*, 7th edition**

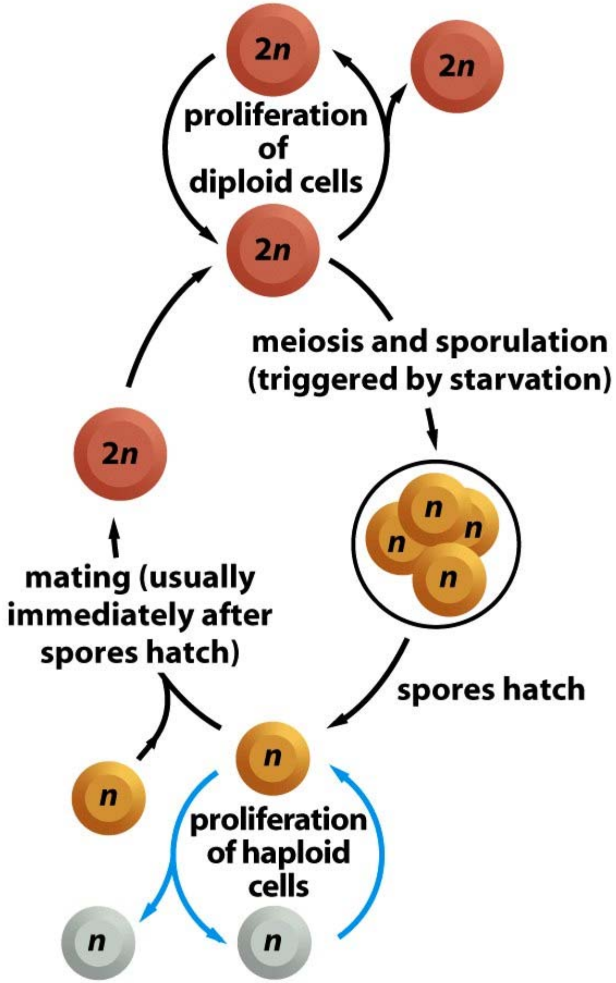
The world of vertebrates is represented by a worm, a fly, a mouse and a human

Use of Yeast as a model system to study cell division

Many genes that control the cell cycle are conserved and interchangeable between yeast and human….

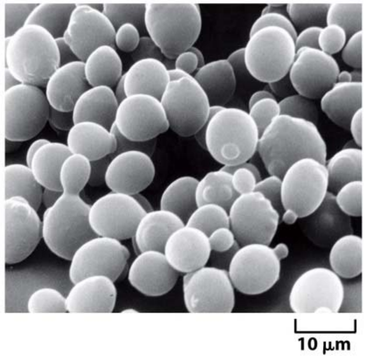


a life cycle for somatic mammalian cell



BUDDING YEAST LIFE CYCLE

Mutations in Yeast led to the identification of key cell cycle proteins



Mutagen,
UV, IR

Yeast cells with largely random mutation

Isolate temperature-sensitive mutants with altered division of haploid yeast Cells

low temperature - **permissive**
mutated protein fold correctly

high temperature - **non-permissive**
mutated protein fold wrongly

- **Isolate** those mutation-defined genes
- **Clone** them,
- **Study** their biochemistry

Use **sequence alignment** to **search** their **human homologs**, usually human homologs can rescue the phenotype caused by these mutants.

Screening for temperature-sensitive mutants

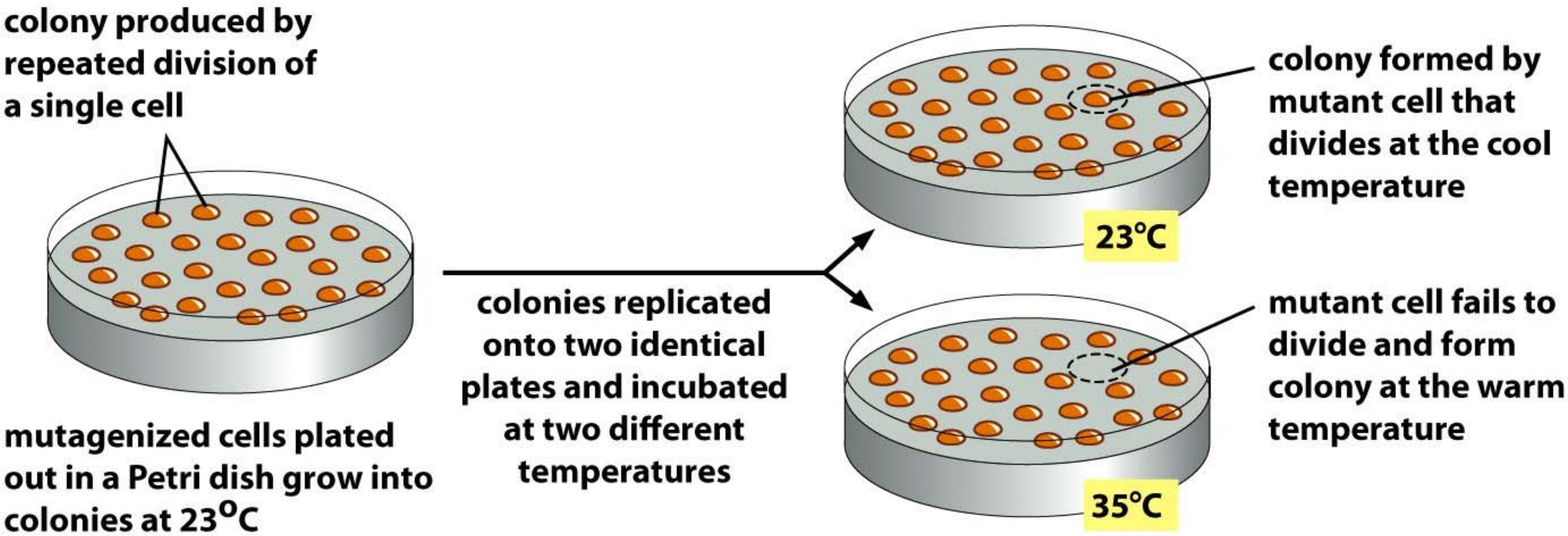
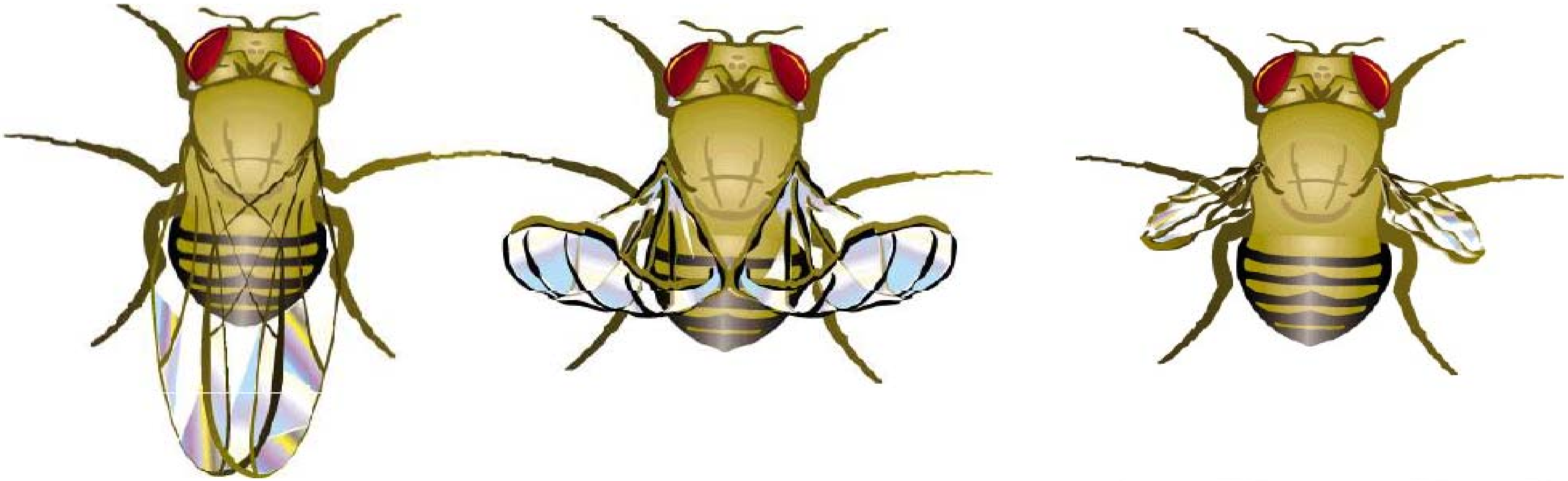


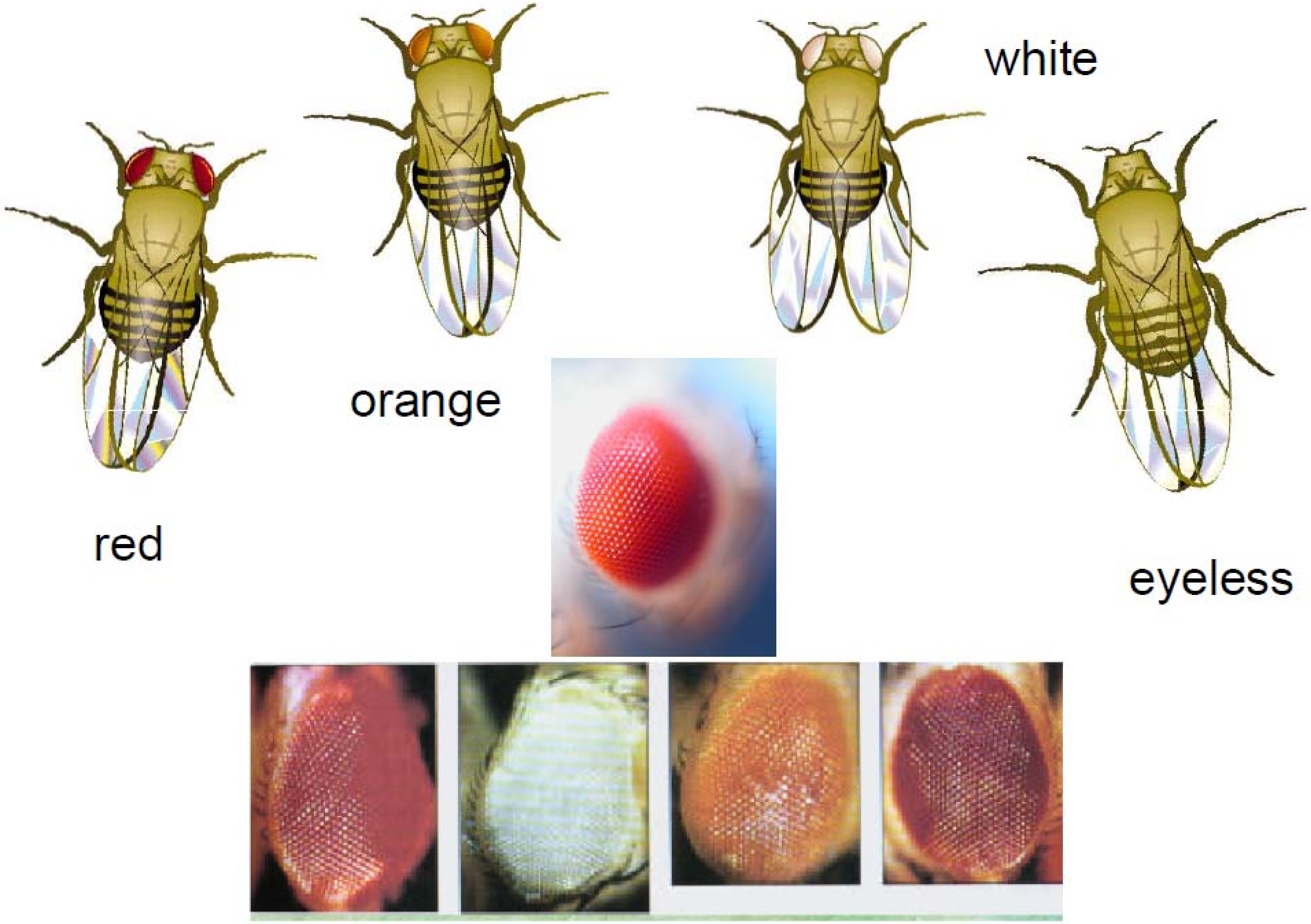
Figure 1-35 Essential Cell Biology 3/e (© Garland Science 2010)

Drosophila melanogaster wing mutations



Normal-winged **Curly-winged** **Short-winged**

Drosophila melanogaster eye color mutations



Summary and thoughts:

1. Think about why you want to study Cell Biology.
2. Understand the theory of cell and the history of cell theory.
3. What are the general differences
   between eukaryotic cells and prokaryotic cells?
4. Understand all cells have constancy in four remarkable aspects.
5. Think about the evolution of life.
6. Understand the common ways of gene evolution.
7. What are the common model systems used in cell biology?