# *Cell and Molecular Biology Concepts and Experiments 8th edition Karp Solutions Manual*

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Chapter 1: Review Questions
Karp, 8th edition

***Section 1.1***

1) When Robert Hooke first described cells, what was he actually looking at?

Answer: Hooke was actually looking at cell walls of dead plant tissue, which he obtained from cork.

2) What are the three components of cell theory?

Answer: The three main components of cell there are (1) all organisms are composed of cells, (2) the cell is the structural unit of life, and (3) cells can only arise by division of pre-existing cells.

***Section 1.2***

1) List the fundamental properties shared by all cells. Describe the importance of each of these properties.

Answer:

- **Alive**. Cells are generally the smallest unit of life. Individual cells can be removed from a plant or animal and grown (sometimes indefinitely) in culture, but this cannot generally be done with individual cell parts.

- **Highly complex and organized**. The complexity means that the cell can perform intricate functions with a great deal of regulation and control. The organization of cells is visible at all levels: atomic, molecular, polymeric, complexes, organellar, and cellular. The organization is important for the function of cells.

- **Genetic Information**. All the genetic information needed by the organism is packaged within the cell.

- **Growth and Reproduction**. Cells are capable of expanding their biomass and producing more cells.

- **Energy**. Cells are able to use energy to perform their functions (either by obtaining it directly from external sources or making it from other energy sources such as the sun).

- **Metabolism**. Cells are capable of performing chemical reactions that would not occur or would only occur slowly outside of the cell.

- **Movement.** All cells are able to move materials within their boundaries and some cells are able to move themselves.

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- **Responsive**. Cells will respond to internal and external stimuli in order to maintain a steady state or homeostasis.

2) Describe the features of cells that suggest that all living organisms are derived from a common ancestor.

Answer: The fact that all cells use DNA as their information storage molecule is the key indicator that all cells descend from a common ancestor. The lack of huge deviation in the genetic sequence of common, ubiquitous housekeeping genes is another indicator. Structures common to all cells such as the RNA-ribosome complex for protein synthesis, or plasma membranes also suggest a common ancestor.

3) What is the source of energy that supports life on Earth? How is this energy passed from one organism to the next?

Answer: Electromagnetic radiation from the sun. Plants convert and store this energy in energy-rich carbohydrates. The energy is passed in the form of other biomolecules from one organism to the next.

***Section 1.3***

1) Compare a prokaryotic and eukaryotic cell on the basis of structural, functional, and metabolic differences.

Answer: Structural Differences: Prokaryotes have a cell envelope enclosing their cell, a naked genome stored in the nucleoid, free ribosomes and no membrane-bound organelle. Eukaryotes have nuclear envelope dividing nucleus from cytoplasm, complex membranous organelles, structurally complex chromosomes, free and membrane-localized ribosomes, complex cytoskeleton with motor proteins, complex flagella and cilia, plant cell walls have cellulose, mitotic spindle, at least two copies of nuclear genome, and three different RNA polymerases.
Functional Differences: Prokaryotes typically divide by binary fission and obtain nutrients using simple diffusion across their cell envelope, and can only modify their genome through mutation or conjugation. Eukaryotes have complex mechanism for cell division (mitosis), are able to ingest fluid and particulates (endocytosis and phagocytosis), and may have sexual reproduction requiring meiosis and fertilization.
Metabolic Differences: Similar metabolic pathways (e.g. glycolysis and TCA cycle) but prokaryotes are capable of surviving in unusual habitats and are also capable of nitrogen fixation.

2) What is the importance of cell differentiation?

Answer: Cell differentiation delegates specific functions to various cell types. This is the shift from pleuripotency to the final cell state. It is typically not reversible.

***Section 1.4***

1) Which group of prokaryotes is best known for containing many extremophiles?

Answer: Archaea.

***Section 1.5***

1) What is the importance of cell differentiation?

Answer: Differentiation allows all of the different cell types in our bodies to be produced, starting from a single cell – the fertilized egg.

***Section 1.7***

1) Why are cells almost always microscopic?

Answer: As a cell increases in size, its surface/volume ratio decreases and the distance between the surface and interior of the cell may increase. If a cell were to grow too large, its surface may not be able to take up materials (such as oxygen or nutrients) at a sufficient rate, or the distance from the surface and the interior of the cell may result in diffusion rates that are too slow to support the cell's activities.

2) If a mitochondrion were 2 µm in length, how many angstroms would it be? How many nanometers? How many millimeters?

Answer: 200 Å; 2000nm; .002 mm.

***Section 1.8***

1) What properties distinguish a virus from a bacterium?

Answer: Viruses are usually smaller than bacteria and are not considered to be organisms or alive. They cannot metabolize or reproduce unless present within a host cell.

2) What types of infections are viruses able to cause?

Answer: Lytic or integrative (pro-viral) infection.

3) Compare and contrast: nucleoid and nucleus; the flagellum of a bacterium and a sperm; an archaebacterium and a cyanobacterium; nitrogen fixation and photosynthesis; bacteriophages and tobacco mosaic virus; a provirus and a virion.

Answer:

- *Nucleoid/nucleus*. Both are ways of organizing a cell's genetic material. A nucleoid is found in prokaryotes and is a non-membranous area containing the cell's genetic material. A nucleus is found in eukaryotes and is a complex membrane-bound structure.

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- *Bacterial flagellum/sperm flagellum*. Both are structures involved in motility but the prokaryotic flagellum is simpler in structure than the eukaryotic flagellum. The flagella of each type of cell also generates movement by a different mechanism.

- *Archaebacterium/cyanobacterium*. Both are prokaryotes. Cyanobacteria are the most complex prokaryotes and are photosynthetic. Archaebacteria are ancient prokaryotes and contain the extremophiles.

- *Nitrogen fixation/photosynthesis*. Both metabolic processes can be carried out by prokaryotes and one group (cyanobacteria) can perform both. Nitrogen fixation involves converting nitrogen gas into reduced forms of nitrogen that can be used by plants. Photosynthesis involved the use of the sun's energy to produce energy-rich carbohydrates.

- *Bacteriophages/tobacco mosaic virus*. Both are types of viruses. Bacteriophages infect bacteria while tobacco mosaic virus infects plants.

- *Provirus/virion*. Both are forms of a virus. A provirus is the name given to the stage when an infecting virus inserts its DNA in the host cell's DNA. A virion refers to the inanimate viral particle and consists of the genetic material of the virus and its surrounding protein capsid.

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# CHAPTER 1

# INTRODUCTION TO THE STUDY OF CELL & MOLECULAR BIOLOGY

Objectives

- List the three tenets of the Cell Theory.
- List the fundamental properties shared by all cells, explaining their importance.
- Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
- Explain how study of the metagenome increases our understanding of prokaryotic diversity.
- Explain the importance of cell differentiation within a eukaryotic organism.
- Explain how various types of stem cells may be useful in combatting human disease.
- Explain why cells are so small.
- Describe the structure of a virus and two mechanisms of viral infection of a host cell.
- Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.

## LECTURE OUTLINE

### Introduction (1.0 – Intro)

I. Cell & molecular biology is **reductionist** – this is based on the view that knowledge of the parts of the whole can explain the character of the whole
   A. The reductionist view can lead to replacement of the wonder & mystery of life by the need to explain everything in terms of the workings of the "machinery" of living systems which many consider a loss
   B. It is hoped that one can replace this loss by an equally strong appreciation for the beauty & complexity of the mechanisms underlying cellular activity

II. Cell biology began as a result of the discovery that curved glass surfaces can bend light & form images
   A. Spectacles were first made in Europe in the 13$^{th}$ century
   B. First compound (double-lensed) microscopes were made by the end of the 16$^{th}$ century; microscopes provide a magnified image of a tiny object
   C. By the mid-1600s, a handful of scientists had used handmade microscopes to uncover a previously unseen world that could not be seen with the naked eye

### The Discovery of Cells (1.1)

I. Robert Hooke (1665), English microscopist (at age 27, became curator of the Royal Society, England's foremost scientific academy); generally credited with the discovery of cells
   A. Described chambers in cork (part of the bark of trees); called them cells (cellulae) since they reminded him of cells occupied by monks living in a monastery
      1. Found them while trying to explain why cork stoppers could hold air in a bottle so effectively; cork is part of the bark of trees
      2. He said ""I took a good clear piece of cork, ....., I cut a piece of it off, and . . . then examining it with a *Microscope*, me thought I could perceive it to appear a little porous . . . much like a Honeycomb."

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3. He called the pores cells

B. Was looking at the empty cell walls of dead plant tissue; no internal structure – walls originally made by the living cells they surrounded

II. Anton van Leeuwenhoek (1665-1675), Dutch seller of clothes & buttons – in spare time, he ground lenses & made simple microscopes of remarkable quality

A. For 50 years, he sent letters to the Royal Society of London describing his microscopic observations; he included in his letters a rambling discourse on his daily habits & the state of his health

B. He was the first to describe living single cells; his results were checked and confirmed by Hooke

1. Saw "animalcules" in pond water darting back & forth (first to do this) using the scopes that he made
2. First to describe various forms of bacteria from tooth scrapings & water in which pepper was soaked

C. His initial letters to the Royal Society describing what he saw were met with skepticism so the Society sent its curator, Robert Hooke, to confirm the observations

1. Hooke confirmed Leeuwenhoek's findings & soon Leeuwenhoek was a worldwide celebrity
2. He was visited in Holland by Peter the Great of Russia and the queen of England

III. 1830s - full & widespread importance of cells realized

A. Matthias Schleiden, German lawyer turned botanist (1838) – concluded that, despite differences in various tissue structures, all plant tissues were made of cells & that plant embryos arise from single cell

B. Theodor Schwann, German zoologist (1839) & colleague of Schleiden's – realized cellular basis of animal life; concluded that plants & animals are similar structures

1. Published a comprehensive report on the cellular basis of animal life

C. Schwann concluded that the cells of plants & animals are similar structures & then proposed the first two tenets of Cell Theory

1. *All organisms are composed of one or more cells.*
2. *The cell is the structural unit of life for all organisms.*

D. However, the Schleiden-Schwann view of cell origin was less insightful - both agreed that cells could arise from noncellular materials —> eventually disproved by others; it took time due to their prominence

1. It took a number of years before observations by other biologists were accepted to demonstrate that cells did not arise in this manner any more than organisms arose by spontaneous generation

E. Rudolf Virchow, German pathologist (1855) – made good case for & added third tenet of Cell Theory derived from his cell division observations; it ran counter to Schleiden-Schwann view of cell origins

1. *Cells can arise only by division from a preexisting cell.*

## Basic Properties of Cells (1.2)

I. Life – most basic property of cells; they are the smallest units to exhibit this property

A. Unlike the parts of a cell, which deteriorate if isolated, whole cells can be removed from a plant or animal & cultured in a lab where they will grow & reproduce for extended periods of time

1. If mistreated, they may die
2. Death can be considered one of the most basic properties of life; only a living entity can die
3. Cells within the body generally die by their own hand, by an internal program that causes cells that are no longer needed or cells that pose a risk of becoming cancerous to eliminate themselves

B. George & Martha Gey, Johns Hopkins Univ. (1951) - first human cell culture (HeLa cells); donor was **He**nrietta **La**cks (from her malignant tumor)

1. Descendants from this sample are still grown in labs today
2. Descended by cell division from this first cell sample

C. Cultured cells are simpler to study than cells in body; cells grown *in vitro* (in culture, outside the body) have become an essential tool of cell & molecular biologists

1. Much of what we know about cells has been obtained using cells grown in lab cultures

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II. Cells are highly complex and organized – complexity is evident when encountered, but hard to describe; think of complexity in terms of order & consistency
   A. If a structure is more complex, a greater number of parts must be in the proper place & there must be less tolerance of errors in the nature & interaction of its parts
      1. Also, more regulation or control must be exerted to maintain the system
      2. Cell activities can be remarkably precise – DNA duplication has error rate <1 mistake every 10,000,000 nucleotides incorporated (most errors quickly fixed by elaborate repair mechanism that recognizes defect)
   B. Each level of structure in cells has a great level of consistency from cell-to-cell – each cell type has a consistent appearance in EM; its organelles have a particular shape & location in all individuals of species
      1. Organelles have consistent macromolecular composition arranged in a predictable pattern
      2. Example: epithelial cells that line the intestine are tightly connected to each other like bricks in wall
         a. Cell apical ends (face intestinal lumen) have long processes (microvilli) that facilitate nutrient absorption
         b. Microvilli project outward from apical surface because they contain internal skeleton made of filaments composed of protein (actin) monomers polymerized in characteristic array
         c. At basal ends, intestinal cells have many mitochondria that provide energy to fuel membrane transport
         d. Each mitochondrion is composed of defined pattern of internal membranes, which, in turn, are made of consistent array of proteins, including the electrically-powered protein that makes ATP
   C. Cells achieve organization at many different levels using physical processes that are essentially random
      1. Even though living cells are highly complex & ordered, it is evident that random (stochastic) events play a critical role in all cellular activities
      2. Many molecules in living cells are in constant state of random movement, propelled by thermal energy from environment; cellshave evolved capacity to utilize this movement in highly directed ways
         a. Proteins are complex molecules made of up to hundreds of amino acids & >100,000 Daltons
         b. Despite huge size, they consist of polypeptide chain that has to fold into precisely defined 3D (native) structure; if it fails to fold properly, the protein will lack meaningful function
      3. Cyrus Levinthal (Columbia U., 1969) – identified certain features of folding process that became known as Levinthal's paradox
         a. He noted that, if protein folding depended solely on random molecular movements, it would require more time than the age of the universe for a protein to fold into its native structure
         b. Paradox is that despite their enormous complexity, proteins actually acquire their native structures in fractions of a second
         c. Protein folding driven by random thermal motion, but in stepwise fashion so that protein folds along pathways in which less formed intermediates guide formation of better-formed later intermediates
         d. Folding pathway allows proteins to rapidly "jump" from one step to next until native structure reached
         e. They depend on random activities, but lead to directed outcomes because they select for intermediate stages that lie on the path leading to the desired outcome
   D. Evolution has moved rather slowly at the levels of biological organization with which cell & molecular biologists are concerned
      1. Humans & cats are very different anatomically, but the cells that make up their tissues & their cell organelles are very similar
      2. Actin filaments & the enzyme that makes ATP are virtually identical to similar structures found in such diverse organisms as humans, snails, yeast & redwood trees
      3. Information obtained from studying cells of one organism often has a direct application to other forms of life
      4. Many of the most basic processes (protein synthesis, conservation of chemical energy, membrane structure, etc.) are remarkably similar in all living organisms

III. Cells possess genetic program & the means to use it (a blueprint); encoded in collection of genes made of DNA & organisms are built according to the information encoded therein

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A. The human genetic program has enough information, if converted to words, to fill millions of pages of text
   1. This vast amount of information is packaged into a set of chromosomes that occupies the space in cell nucleus, hundreds of times smaller than the dot on an *i*
B. Genes are more than a storage locker for information; they are the blueprint for constructing cellular structures, the directions for running cellular activities & the program for making more of themselves
C. Gene molecular structure allows for changes in genetic information (mutations) that lead to variation among individuals & forms the basis of biological evolution

IV. Cells are capable of producing more of themselves - mitosis and meiosis
A. Cells reproduce by division, a process whereby "mother" cell contents are distributed into 2 "daughter" cells
B. Before division, genetic material is faithfully duplicated; each daughter cell gets a complete & equal share of genetic information
C. Usually, daughter cells have roughly equal volume; however, during egg production, one cell gets nearly all of the cytoplasm & even though it receives only half of the genetic material

V. Cells acquire & use energy (constant input) to develop & maintain complexity – photosynthesis, respiration; every biological process requires an input of energy
A. Virtually all energy needed by life on Earth's surface arrives from sun in form of electromagnetic radiation
B. This energy is trapped by light-absorbing pigments in the membranes of photosynthetic cells
C. Light energy is turned to chemical energy by photosynthesis; it is stored in energy-rich carbohydrates (sucrose or starch)
D. Most animal cells get energy prepackaged, often in form of glucose (released to blood by liver in humans); once in blood, it circulates through body delivering chemical energy to all cells in the body
E. Once in cell, glucose is disassembled; most of its energy is stored in the readily available form of (usually) ATP & used later to run all of the cell's energy-requiring activities
   1. Cells expend an enormous amount of energy simply breaking down & rebuilding the macromolecules & organelles of which they are made
   2. This continual turnover maintains the integrity of cell components in face of inevitable wear & tear to which they are subjected & enables the cell to respond rapidly to changing external conditions

VI. Cells carry out a variety of chemical reactions like tiny chemical plants
A. Even the simplest bacterial cell is capable of hundreds of different chemical transformations, none of which occurs at any significant rate in the inanimate world
B. Virtually all chemical changes happening in cells require **enzymes** to greatly increase the reaction rates
C. The sum total of chemical reactions in a cell represents the cell's **metabolism**

VII. Cells engage in numerous mechanical activities based on dynamic, mechanical changes in cells, many of which are initiated by changes in the shape of "motor" proteins (require constant energy to keep working):
A. Materials are transported from place to place
B. Structures are assembled and then rapidly disassembled
C. Cells move from place to place

VIII. Cells able to respond to stimuli whether organisms are uni- or multicellular - have receptors that sense environment & initiate responses (protists move away from object in path or toward nutrient source)
A. Most cells are covered with receptors that interact in highly specific ways with substances in environment
   1. Receptors bind to hormones, growth factors, extracellular materials, substances on surfaces of other cells
   2. Allow ways for external agents to evoke specific responses in target cells
B. Cells may respond to specific stimuli by:
   1. Altering their metabolic activities
   2. Preparing for cell division
   3. Moving from one place to another, or

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4. Even committing suicide

IX. Cells are capable of self-regulation
   A. Cells are *robust* meaning hardy or durable, because they are protected from dangerous fluctuations in composition & behavior
      1. If fluctuations occur, specific feedback circuits are activated that serve to return the cell to the appropriate state
      2. In addition to requiring energy, maintaining a complex, ordered state requires constant regulation
   B. Importance of regulatory mechanisms is most evident when they break down
      1. Failure of cell to correct error in DNA replication —> may lead to debilitating mutation
      2. Breakdown in growth-control safeguards —> may lead to cancer cell & maybe death of whole organism
   C. Ex.: Hans Driesch, German embryologist (1891) - separate first 2 or 4 cells in sea urchin embryo —> each produces normal embryo; the cells regulated their activities to make whole embryos
   D. Cell processes are a series of ordered steps (like assembly line) – the information for these steps & product design reside in nucleic acids & construction workers for these processes/designs are primarily proteins
      1. In cell, the workers act without the benefit of conscious direction
      2. Each step in process must occur spontaneously so that the next step is automatically triggered
      3. Each type of cell activity requires unique set of highly complex molecular tools & machines, the products of eons of natural selection & biological evolution
   D. Primary goal of cell/molecular biologists is to understand the molecular structure & role of each component in a particular activity, the ways in which they interact & mechanisms by which interactions are regulated

X. Cells evolve
   A. It is presumed that cells evolved from some type of precellular life form, which, in turn, evolved from nonliving organic molecules that were present in the primordial seas
   B. While cell origin is shrouded in near-total mystery, the evolution of cells can be studied by examining organisms that are alive today
      1. Observe bacterial cell in human intestinal tract & cell that is part of lining of that tract; you would be struck by their differences
      2. Yet both of these cells (& all cells) share many features (common genetic code, plasma membrane & ribosomes)
      3. According to one tenet of modern biology, all living organisms have evolved from a single, common ancestral cell that lived >3 billion years ago
         a. Because it gave rise to all living organisms we know of, this ancient cell is often called the *last universal common ancestor (or LUCA)*
         b. Structures shared by these two distantly related cells (similar plasma membranes, ribosomes) must have been present in the ancestral cell
   C. Evolution is not simply an event of the past, but an ongoing process that continues to modify cell properties that will be present in organisms yet to appear

## Characteristics That Distinguish Prokaryotic and Eukaryotic Cells (1.3)

I. With advent of EM, 2 basic cell classes were distinguished by size & types of internal structures (**organelles**); represents one of most fundamental evolutionary divisions in biological world (there are no known intermediates)
   A. Prokaryotes (*pro* - before; *karyon* - nucleus) – all bacteria, cyanobacteria (blue-green algae); structurally simpler; we are not sure when prokaryotic cells first appeared on Earth
      1. Evidence of prokaryotic life obtained from rocks ~2.7 billion year old rocks (Australia, S. Africa); prokaryotes now living seem very similar to those fossilized in rocks
         a. They were the sole life on planet for nearly 2 billion years before the first eukaryote

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2. These rocks also contain complex organic molecules characteristic of particular types of prokaryotic organisms, including cyanobacteria; unlikely that such molecules could have been made abiotically
3. Cyanobacteria almost certainly appeared by 2.4 billion years ago, because that is when the atmosphere became infused with molecular oxygen ($O_2$), a byproduct of their photosynthesis

B. Eukaryotes (*eu* – true; *karyon* - nucleus) - structurally more complex; protists, fungi, plants, animals
1. Their origin is also uncertain – complex multicellular animals appear suddenly in fossil record ~600 million years ago
   a. But there is considerable evidence that simpler eukaryotes were present >1 billion years earlier
2. It is clear that life arose quickly after the formation of Earth & the cooling of its surface; & that it took longer for the subsequent evolution of complex plants & animals

II. A comparison of prokaryotes & eukaryotes reveals many differences & similarities – shared properties reflect the fact that eukaryotes almost certainly evolved from prokaryotic ancestors; because of common ancestry:
A. Both types of cells encode genetic information in DNA using an identical genetic language or code
B. Both types of cells share a common set of metabolic pathways (glycolysis, TCA cycle)
C. Both types of cells share many common structural features – similarly constructed plasma membrane that serves as selectively permeable barrier & often protective cell walls (same function, different compositions)
D. Similar mechanisms for transcription & translation of genetic information, including similar ribosomes
E. Similar apparatus for conservation of chemical energy as ATP (located in plasma membrane of prokaryotes & mitochondrial membrane of eukaryotes)
F. Similar mechanism of photosynthesis (between cyanobacteria & green plants)
G. Similar mechanism for synthesizing & inserting membrane proteins
H. Proteasomes (protein digesting structures) of similar construction (between archaeabacteria & eukaryotes)

III. Characteristics that distinguish prokaryotic & eukaryotic cells - eukaryotic cells are much more complex internally (structurally and functionally) than prokaryotes; can be seen easily in EM
A. Eukaryotes have membrane-bound nucleus with nuclear envelope containing complex pore structures & other organelles; divides eukaryotic cells into nucleus & cytoplasm
1. Prokaryotes have nucleoid (poorly demarcated cell region that lacks a boundary membrane separating it from surrounding cytoplasm) & no membrane-bound organelles
2. Despite importance often placed on nucleus as primary criterion for distinguishing prokaryotes & eukaryotes, a group of prokaryotes is reported to have membrane surrounding their genetic material
3. This provides good example of difficulty in making sweeping generalizations that apply to all groups of living organisms

B. Prokaryotes – contain relatively small amounts of DNA (~600,000 base pairs [bp] to nearly 8 million bp; ~0.225 – 3 mm); 8 million bp equals DNA molecule nearly 3 mm long
1. Encodes between ~500 to several thousand proteins (1 mm of DNA = ~3 x $10^6$ base pairs)
2. Simplest eukaryotes (4.6 mm or 12 million bp in baker's yeast encoding ~6200 proteins) have slightly more DNA than prokaryotes; most eukaryotes contain considerably more DNA (genetic info)

C. Both prokaryotic & eukaryotic cells have DNA-containing chromosomes: eukaryotes - a number of separate chromosomes, each with single linear DNA molecule; most prokaryotes - a single circular chromosome
1. Unlike prokaryotes, eukaryote chromosomal DNA is tightly associated with proteins to form a complex nucleoprotein material known as **chromatin**
2. Eukaryotic chromosomes are also capable of compacting into mitotic structures

D. Cytoplasm of the 2 types of cells is also different – eukaryotic cytoplasm is filled with a great diversity of structures; apparent in any EM of nearly any plant or animal cell
1. Even yeast, the simplest eukaryote, is much more complex structurally than an average bacterium even though the two have a similar number of genes
2. Eukaryotes contain an array of membrane-bound organelles that divide cytoplasm into compartments within which specialized activities take place

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3. Prokaryotic cell cytoplasm is essentially devoid of membranous structures; complex photosynthetic membranes of cyanobacteria & infolded bacterial mesosomes are major exceptions to this generalization

IV. Some examples of eukaryotic organelles follow:
- A. Mitochondria (plants & animals) – make chemical energy available to fuel cell activities; specialized cytoplasmic organelle for doing aerobic respiration
- B. Endoplasmic reticulum (plants & animals) – where many of a cell's lipids & proteins are manufactured
- C. Golgi complexes (plants & animals) – sorts, modifies, & transports materials to specific cellular desinations
- D. Variety of simple membrane-bound vesicles of varying dimension (plants & animals)
- E. Chloroplasts (plants) – specialized cytoplasmic organelle that is the site of photosynthesis
- F. Single large vacuole (plants) – occupies most of the volume of the cell
- G. Lysosomes – contains hydrolytic enzymes & carries out hydrolytic gestation; endosomes – vesicles bringing materials into cell to often be digested by lysosomes
- H. Peroxisomes & glyoxysomes

V. Cytoplasmic membranes of eukaryotes form a system of interconnected channels & vesicles that function in the transport of substances from one part of cell to the other, as well as between cell interior & environment
- A. Because of their small size, directed intracytoplasmic communication is less important in prokaryotes, where the necessary movement of materials can be accomplished by simple diffusion
- B. Eukaryotic cells also contain numerous structures lacking a surrounding membrane
  1. Elongated tubules & filaments of cytoskeleton that participate in cell contractility, movement, & support
     a. Long thought prokaryotes lack cytoskeleton, but primitive cytoskeletal filaments recently seen in bacteria
     b. Still fair to say prokaryotic cytoskeleton much structurally/functionally simpler than that of eukaryotes
  2. Both prokaryotes & eukaryotes have ribosomes serving as workbenches on which cell proteins are made
     a. They have considerably different dimensions (prokaryote ribosomes smaller with fewer components than those of eukaryotes (but they essentially have same function with similar mechanisms)
  3. Cytoplasm near thin edge of single-celled eukaryotic organism is region where membrane-bound organelles tend to be absent, but, in general, the cytoplasm of a eukaryotic cell is extremely crowded
     a. This leaves very little space for the soluble phase of the cytoplasm called **cytosol**
  4. Both eukaryotes & prokaryotes may be surrounded by rigid, nonliving cell wall that protects, but their chemical composition is very different

VI. No mitosis or meiosis in prokaryotes (binary fission instead); prokaryotes proliferate faster (double in 20 - 40 minutes; they exchange genetic information via conjugation)
- A. In eukaryotes, duplicated chromosomes condense into compact structures; segregated by mitotic spindle (elaborate; contains microtubules); allows daughter cells to get equivalent array of genetic material
- B. In prokaryotes, no chromosome compaction & no spindle to separate the genome copies after replication; DNA is duplicated & copies are separated by growth of an intervening cell membrane
  1. It was once thought that the 2 copies are separated by attaching the DNA to the cell surface allowing the growth of the cell membrane to pull them apart
  2. However, live cell imaging showed that DNA separates faster than the cell grows; the precise mechanism by which prokaryotes segregate their genomes remains an open question
  3. Some current models are based on regulated compaction or folding of the DNA so that the 2 copies would fold into two separate masses, thus separating them
- C. For the most part, prokaryotes do not reproduce sexually; they contain only one copy of their single chromosome & have no processes comparable to meiosis, gamete formation or true fertilization, but…..
  1. Some are capable of **conjugation**, in which a piece of DNA is passed from one cell to another
  2. However, the recipient almost never gets a whole chromosome from donor; the condition in which the recipient cell contains both its own & its partner's DNA is fleeting; cell soon reverts to single chromosome
  3. Not true sexual reproduction

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D. Prokaryotes are not as efficient as eukaryotes in exchanging DNA with other members of their own species, but are, however, more adept than eukaryotes at picking up & incorporating foreign DNA from environment
   1. This has had considerable impact on microbial evolution

VII. Eukaryotes have a variety of complex locomotor mechanisms; those of prokaryotes are relatively simple
   A. Prokaryotes may move using a thin, rotating protein filament (**flagellum**) protruding from the cell; rotations (can exceed 1000 times/sec) exert pressure against surrounding fluid propelling cell through medium
   B. Certain eukaryotes (many protists & sperm cells) have much more complex flagella with different mechanism (also have cilia, pseudopodia); they are not the simple protein filaments of bacteria

VIII. Prokaryotes are not inferior
   A. They have remained on Earth for more than 3 billion years
   B. They live on & in eukaryotic organisms, including humans; trillions cling of them cling to the outer surface of your body & feast on the nutrients within your digestive tract
   C. We think of them as individual, solitary creatures, but recent insights have shown that they live in complex, multispecies communities called **biofilms**
      1. The layer of plaque that grows on our teeth is an example of a biofilm
      2. Different cells in a biofilm may carry out different specialized activities, not unlike the cells in a plant or animal
   D. Metabolically, they are very sophisticated, highly evolved organisms
      1. Bacterium like *Escherichia coli*, a common inhabitant of both human digestive tract & lab culture dish, can live & prosper in a medium containing 1 or 2 low-MW organic compounds & a few inorganic ions
      2. Other bacteria can live on a diet consisting solely of inorganic substances
         a. One species has been found in wells >1000 meters below Earth's surface living on basalt rock & molecular hydrogen ($H_2$) produced by inorganic reactions
   E. Even the most metabolically talented cells in a human require a variety of organic compounds (vitamins, etc.) & other essential substances that they cannot make on their own
      1. In fact, many of these essential dietary ingredients are made by bacteria that normally live in our large intestine

## Types of Prokaryotic Cells (1.4)

I. Prokaryotes are split into 2 major taxonomic groups or domains – Archaea (archaebacteria) & Bacteria (or eubacteria)

II. Domain Archaea (archaeons or archaebacteria) – thought to include our closest living prokaryotic ancestors; more closely related to eukaryotes than they are to the Bacteria (eubacteria)
   A. They include several groups of organisms whose evolutionary ties to one another are revealed by similarities in the nucleotide sequences of their nucleic acids
   B. Best known Archaea live in extremely inhospitable environments (extremophiles) & they include:
      1. Methanogens - capable of converting $CO_2$ & $H_2$ gases into methane ($CH_4$) gas
      2. Halophiles – prokaryotes that live in extremely salty environments (Dead Sea or certain deep-sea brine pools that possess a salinity equivalent to 5M $MgCl_2$)
      3. Acidophiles – acid-loving prokaryotes that thrive at pHs as low as 0, such as that found in the drainage fluids of abandoned mine shafts
      4. Thermophiles – prokaryotes that live at very high temperatures, including:
         a. Hyperthermophiles - live in hydrothermal vents of ocean floor; latest record holder in group is "strain 121," since it is able to grow & divide in superheated water at 121°C

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b. 121°C is the temperature used to sterilize surgical & laboratory equipment in an autoclave

C. Recent analyses of soil & ocean microbes indicate that many members of the Archaea are also at home in habitats of normal temperature, pH, & salinity

III. Domain Bacteria (eubacteria) – all prokaryotes other than those of the Archaea; includes the smallest known cells, the mycoplasma & the cyanobacteria

A. Bacteria are present in every conceivable habitat on earth – from the permanent Antarctic ice shelf to the driest African deserts to internal confines of plants & animals

1. Bacteria have even been found living in rock layers found several kilometers beneath the Earth's surface
2. Some bacterial communities have been cut off from life on the surface for >100,000,000 years
3. Example: Mycoplasma - smallest living cells (0.2 µm dia); the only known prokaryotes to lack a cell wall & to contain a genome with fewer than 500 genes
4. Example: Cyanobacteria (formerly blue-green algae) – the most complex prokaryotes
   a. They contain elaborate cytoplasmic membrane arrays, which are sites of photosynthesis; very similar to chloroplast photosynthetic membranes in plant cells
   b. As in plants, cyanobacteria photosynthesis is done by splitting $H_2O$ molecules; releasing molecular oxygen ($O_2$); filled world with $O_2$ & need few resources to survive

B. Many cyanobacteria also do **$N_2$ fixation** - convert $N_2$ gas into reduced nitrogen forms (e.g., ammonia or $NH_3$) that are used to make nitrogen-containing organic compounds like amino acids & nucleotides

1. Those species capable of both photosynthesis & nitrogen fixation can survive on the barest of resources (light, $N_2$, $CO_2$, $H_2O$)
2. Thus, it is not surprising that cyanobacteria are the first to colonize bare rocks left lifeless by a scorching volcanic eruption
3. They also live inside the hairs of polar bears; responsible for the unusual greenish color of their coat

IV. Prokaryotic diversity

A. Mostly, microbiologists are familiar only with the microorganisms they can grow in a culture medium

1. When patient suffers from respiratory or urinary tract infection & sees doctor, one of first steps taken is to culture the pathogen
2. Once cultured, it can be identified & the proper treatment prescribed
3. It is relatively easy to culture *most* disease-causing prokaryotes, but the same is not true for those living free in nature

B. Due to culturing difficulties, their limited visibility in the light microscope & morphology that is not very distinctive, roughly 6000 prokaryotic species have been identified by traditional techniques

1. This is <0.1% of the millions of prokaryotic species thought to exist on Earth
2. Our appreciation for prokaryotic diversity has increased through the introduction of molecular techniques that do not require the isolation of a particular organism

C. To study prokaryote diversity (say in upper levels of Pacific off CA coast), cells are concentrated from ocean water, their DNA extracted & DNA sequences analyzed; culturing such organisms would prove largely futile

1. All organisms share certain genes (like genes for rRNAs or some metabolic pathway enzymes)
2. However, sequences of these genes vary considerably species to species (basis of biological evolution)
3. Carefully analyze the variety of sequences for a particular gene in habitat —> tells you directly the diversity of species living in that habitat
4. Recent sequencing techniques have gotten so rapid & cost-efficient that virtually all of the genes present in microbes of a given habitat can be sequenced, generating a collective genome or **metagenome**
5. This approach can provide information about the types of proteins these organisms manufacture & thus about many of the metabolic activities in which they engage

D. Same molecular strategies are now being used to explore the diversity of microbes living on or within our bodies in habitats like intestinal tract, mouth, vagina & skin

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1. Ex.: subgingival cavities of mouth; these are spaces between teeth & gums & are home to one of best-studied microbial communities; include bacteria that cause tooth decay, gingivitis & heart disease
2. The collection of microbes that live on our bodies, known as the **microbiome**, is the subject of several international research efforts aimed at identifying & characterizing these organisms
   a. Being done for people of different age, diet, geography & state of health
3. Already demonstrated, for example, that obese & lean humans have markedly different populations of bacteria in their digestive tracts
   a. As obese individuals lose weight, their bacterial profile shifts toward that of leaner individuals
   b. A recent study of fecal samples from 124 people of varying weight revealed the presence within the collective population of >1000 different species of bacteria
   c. Taken together, these microbes contained >3 million distinct genes, ~150 times as many as the number present in the human genome
   d. Among the functions of proteins encoded by these microbial genomes are the synthesis of vitamins, breakdown of complex plant sugars & the prevention of growth of pathogenic organisms

E. By using sequence-based molecular techniques, biologists have found that most habitats on earth are teeming with previously unidentified prokaryotic life
1. >90% of these organisms are now thought to live in subsurface sediments well beneath oceans & upper soil layers; not long ago (about a decade), deeper sediments were thought to be only sparsely populated
2. Nutrients can be so scarce in some of these deep sediments that microbes living there are thought to divide only once every several hundred years
3. Carbon sequestered in world's prokaryotes is roughly comparable to the total carbon in world's plants

## Types of Eukaryotic Cells (1.5)

I. In many ways, the most complex eukaryotic cells are among the single-celled (unicellular) protists
A. Protists - do everything an organism must do to survive in single cell – sense the environment, trap food, expel excess fluid, evade predators; this is one evolutionary pathway
B. Alternate pathway is multicellular organisms that exhibit **differentiation** - different activities conducted by different types of specialized cells; this division of labor among cells provides a number of advantages
1. A fertilized human egg progresses through a course of embryonic development that leads to the formation of ~250 distinct types of differentiated cells (digestive gland, muscle, bone, etc.)
2. Differentiation pathway followed by each embryonic cell depends primarily on the signals it receives from the surrounding environment; these signals, in turn, depend on position of cell within the embryo
3. Researchers are learning how to control the process of differentiation in the culture dish & applying this knowledge to the treatment of complex human diseases
C. As a result of differentiation, different types of cells acquire a distinctive appearance & contain unique materials (skeletal muscle, cartilage cells, red blood cells, etc.)
1. Despite their many differences, the various cells of a multicellular plant or animal are composed of similar organelles
2. Mitochondria are found in essentially all types of cells, but sometimes they have rounded shape, or they are highly elongated & thread-like
3. In each case, number, appearance & location of various organelles can be correlated with activities of particular cell type (orchestral pieces – all have same notes, but varying arrangements, sound different)

II. Cell & molecular biology research focuses on a small number of "representative" or **model organisms**
A. Living organisms are highly diverse & results obtained from a particular experimental analysis may depend on the particular organism being studied
B. It is hoped that a comprehensive body of knowledge built on these studies will provide a framework to understand those basic processes that are shared by most organisms, especially humans
1. This is not to suggest that many other organisms are not widely used in study of cell & molecular biology

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C. Nonetheless, 6 model organisms (1 prokaryote; 5 eukaryotes) get the most attention; each has specific advantages that make it particularly useful as a research subject for answering certain types of questions
   1. *Escherichia coli (E. coli)* - a bacterium
   2. *Saccharomycese cerevisiae* - a budding yeast (more commonly known as baker's or brewer's yeast)
   3. *Arabadopsis thaliana* – a mustard plant (a flowering plant)
   4. *Caenorhabditis elegans* – a nematode
   5. *Drosophila melanogaster* – a fruit fly
   6. *Mus musculus* – a mouse

D. The book usually concentrates on results obtained from studies on mammalian systems, mostly on the mouse & on cultured mammalian cells, because these findings are more applicable to humans
   1. A large portion of what we know about mammalian cells was first discovered by experiments in other model organisms that are easier to work with
   2. Humans are very similar to these much smaller & simpler organisms

III. The specific advantages of each organism

A. *Escherichia coli* – rod-shaped bacterium; lives in digestive tract of humans & other mammals; much of basic molecular biology of cells first worked out in *E. coli* (replication, transcription, translation, etc.)

B. *Saccharomycese cerevisiae* – the least complex of the eukaryotes commonly studied, yet it contains a surprising number of proteins homologous to proteins in human cells
   1. Such proteins usually typically have conserved function in the two organisms
   2. It has a small genome encoding ~6200 proteins
   3. Can be grown in haploid state (1 copy of each gene per cell, rather than 2 as in most eukaryotic cells)
   4. Can be grown under either aerobic ($O_2$-containing) or anaerobic ($O_2$-lacking) conditions

C. *Arabadopsis thaliana* – a member of a genus of mustard plants; it has an unusually small genome (120 million base pairs) for a flowering plant
   1. It has a rapid generation time, large seed production & grows to a height of only a few inches

D. *Caenorhabditis elegans* – a microscopic-sized nematode; it consists of a defined number of cells (roughly 1000), each of which develops according to a precise pattern of cell divisions
   1. The animal is easily cultured and has a transparent body wall, a short generation time & a facility for genetic analysis
   2. The researchers who pioneered the study of its larval nervous system won the 2002 Nobel Prize

E. *Drosophila melanogaster*- it is a small, but complex, eukaryote that has been a favored animal for genetic study for nearly 100 years
   1. It is well suited for the study of the molecular biology of development & the neurological basis of simple behavior
   2. Certain larval cells have giant chromosomes, whose individual genes can be identified for studies of evolution & gene expression

F. *Mus musculus* – it is the common house mouse & is easily kept & bred in the laboratory
   1. Thousands of different genetic strains have been developed, many of which are stored simply as frozen embryos due to lack of space to house the adult animals
   2. The "nude mouse" develops without a thymus gland & therefore is able to accept human tissue grafts that are not rejected

## *The Sizes of Cells and Their Components (1.7)*

I. Units of linear measure most often used to describe cell structures

A. Micrometers (µm; $10^{-6}$ m), nanometers (nm; $10^{-9}$ m)

B. Ångstroms (Å; angstroms; $10^{-10}$ m) – often used by molecular biologists for atomic dimensions; ~1 Å = roughly the diameter of H atom; also equals 0.1 nm

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II. Examples of dimensions of cells and cell components; large biological molecules (i.e., macromolecules) are described in either angstroms or nanometers
   A. Typical globular protein (myoglobin) - ~ 4.5 nm x 3.5 nm x 2.5 nm
   B. Highly elongated proteins (collagen, myosin) - >100 nm in length
   C. DNA - ~2 nm in width
   D. Large molecular complexes (ribosomes, microtubules, microfilaments) - 5 - 25 nm in diameter
      1. These complexes are remarkably sophisticated nanomachines that can perform a diverse array of mechanical, chemical, & electrical activities
   E. Cells & organelles are more easily defined in micrometers
      1. Nuclei - ~5 - 10 µm in diameter; mitochondria - ~2 µm in length
      2. Bacteria (prokaryotic cells) - ~1 to 5 µm in length; eukaryotic cells - ~10 to 30 µm in length

III. Why are most cells so small?
   A. Most eukaryotic cells have single nucleus containing only 2 copies of most genes
      1. Thus, cells can only produce a limited number of mRNAs in a given amount of time, because genes serve as templates for mRNA production
      2. The larger a cell's volume is, the longer it will take to make the number of mRNAs the cell needs
   B. As a cell increases in size, the surface area/volume ratio decreases (do the math with a small & large cube)
      1. The ability of a cell to exchange substances with its environment is proportional to its surface area
      2. If a cell grows beyond a certain size, the surface area/volume ratio gets too small; surface area is not sufficient to take up substances needed to support metabolism ($O_2$, nutrients, etc.) or get rid of wastes
   C. How do large cells get around the surface area/volume problems? - examples
      1. Cells specialized for solute absorption (e.g., intestinal epithelium) typically possess microvilli to greatly increase the surface area available for exchange
      2. Another strategy to get around surface area/volume problem - interior of large plant cell is typically filled by large, fluid-filled vacuole rather than metabolically active cytoplasm
      3. Ostrich egg & others - little living protoplasm spread over top of lots of inert yolk nutrient
      4. Giraffe (& other large animal) nerve cells - very long, but very small diameter
   D. Cells depend to a large degree on random movement of molecules (**diffusion**); as cell gets larger, it takes too long for diffusion to move substances in & out of active cell (ex.: $O_2$ diffusing into cell)
      1. Time required for diffusion is proportional to the square of the distance to be traversed
      2. For example, $O_2$ requires 100 µsec to diffuse 1 µm, but $10^6$ times longer to diffuse 1 mm
      3. As a cell becomes larger, the distance from surface to interior gets larger & the diffusion time required to move things in & out of a metabolically active cell becomes prohibitively long
   E. Despite these constraints, some eukaryotic cells can be extremely large
      1. The free-living, single-celled organism *Stentor coeruleus*, which lives in freshwater ponds, grows to be >1mm long & the giant, single-celled green alga Acetabularia is >10 cm long
      2. The gargantuan, sigle-celled green alga Caulerpa can grow to a length of several meters & contains millions of nuclei in a common cytoplasm
      3. Examples of large cell size are not restricted to such strange organisms, however; humans have some examples; neurons send out extremely long processes
         a. Motor neurons in human spinal cord send out axons that can be a meter long

## Viruses and Viroids (1.8)

I. There are pathogens smaller &, presumably, simpler than smallest bacteria; called **viruses** – reasoning below
   A. Late 1800s – Pasteur & others thought infectious diseases caused by bacteria, but another agent soon found
   B. Studies of tobacco mosaic disease & hoof-and-mouth disease in cattle pointed to the existence of another type of infectious agent (ex.: tobacco mosaic disease)
      1. Sap from sick tobacco plant gave other healthy plants mosaic disease, while containing no bacteria

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2. Sap filtrate was still infective if forced through filter with pores smaller than the smallest known bacteria – Dmitri Ivanovsky (Russian biologist)
    a. He concluded in 1892 that some diseases were caused by even smaller & simpler pathogens than the smallest known bacteria; these pathogens became known as **viruses**
3. Infectious agent could not be grown in culture, unless living plant cells were also present

C. Wendell Stanley, Rockefeller Institute (1935) - tobacco mosaic virus (TMV) responsible for tobacco mosaic disease, a rod-shaped particle was crystallized & found to be infective
1. Substances that form crystals have a highly ordered, well-defined structure & are vastly less complex than the simplest cells; he mistakenly concluded that TMV was a protein
2. Now know that TMV is a single RNA molecule surrounded by a helical shell made of protein subunits

D. Viruses are responsible for many human diseases & some cancers (AIDS, polio, influenza, ebola, cold sores, measles, a few types of cancers)

E. Viruses occur in a wide variety of very different shapes, sizes & constructions, but all of them share certain common properties

II. Common virus properties - not considered living since need host to reproduce, metabolize, etc.

A. All viruses are obligatory intracellular parasites (must reproduce in host cell [plant, animal, bacteria], depending on specific virus); they are macromolecular aggregates & inanimate particles
1. Alone, they are unable to reproduce, metabolize or carry on other life-associated activities
2. Thus, they are not considered to be organisms & not considered to be alive
3. Once it has attached & passed through membrane, its genetic material can alter host cell activities

B. Outside of a living cell, the virus exists as particle or virion, essentially a macromolecular package
1. Has small amount of genetic material (single or double-stranded, DNA or RNA, depending on virus)
2. Remarkably, they can have as few as 3 or 4 different genes, but some may have as many as several hundred

C. Genetic material of a virion is surrounded by a protein capsule (**capsid**); efficient (need only a few genes to make capsid)
1. Virions are macromolecular aggregates, inanimate particles that, by themselves, cannot reproduce, metabolize or do any activities associated with life; not considered organisms & not described as alive
2. Viral capsids are generally made up of a specific number of subunits
3. There are numerous advantages to construction by subunits, one of the most apparent being an economy of genetic information
4. If a viral coat is made of many copies of one protein (like TMV) or a few proteins (as are coats many other viruses), virus needs only one or a few genes to code for its protein container
5. Capsid subunits are often organized into polyhedron (a structure having planar faces [ex.: 20-sided **icosahedron**]) like adenovirus, which causes mammalian respiratory infections

D. Many animal viruses have capsid surrounded by lipid-containing outer envelope derived from modified host cell membrane as virus buds from host-cell surface (ex.: human immunodeficiency virus [HIV] - AIDS)

E. Bacterial viruses (**bacteriophages**) are among the most complex – T bacteriophages have polyhedral head (contains DNA), cylindrical stalk (injects DNA into bacterium) & tail fibers (attach to bacteria)
1. Altogether it looks like the lunar landing modules
2. They were used in key experiments that revealed genetic material structure & properties
3. They are also the most abundant biological entities on Earth

F. Viruses have surface proteins that bind to particular host cell surface component (specificity)
1. HIV - glycoprotein of 120,000 daltons MW (gp120) interacts with specific protein (CD4) on surface of certain white blood cells, facilitating virus entry into host cell
    a. One dalton is equivalent to one unit of atomic mass, the mass of a single H atom
2. Interaction between viral & host proteins determines the specificity of the virus (the types of host cells that the virus can enter & infect
3. Viral & host protein interaction determines virus specificity, the hosts it can enter & infect

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G. Some viruses have a wide **host range**, being able to infect cells from a variety of different organs or host species, like rabies that infects many different types of mammalian hosts, like dogs, bats & humans
H. Most viruses, however, have a relatively narrow host range (certain cells of certain hosts, like human cold & influenza viruses, which are only able to infect human respiratory epithelium cells)
   1. A change in host-cell specificity can have striking consequences
   2. This is illustrated by the 1918 influenza pandemic, which killed >30 million people worldwide

III. The 1918 influenza pandemic – the virus was especially lethal in young adults who do not normally fall victim to influenza
A. In fact, the 675,000 deaths from the flu in US, temporarily dropped average life expectancy by several years
B. Researchers have, in the past few years, determined the genomic sequence of the virus responsible for this pandemic & reconstituted the virus in its full virulent state – acclaimed & controversial
   1. Done by isolating the viral genes (part of a genome consisting of 8 separate RNA molecules encoding 11 different proteins) from preserved tissues of victims who had died from it 90 years earlier
   2. Best preserved samples obtained from a Native-American woman buried in the Alaskan permafrost
C. The sequence of the 1918 virus suggested that the pathogen had jumped from birds to humans
   1. Although virus had accumulated a considerable number of mutations, adapting it to a mammalian host, it had never exchanged genetic material with that of a human influenza virus as was thought likely
D. Analysis of the 1918 virus' sequence has provided some clues to explain why it was so deadly & how it spread so efficiently from one human to another
   1. Using the genomic sequence, the 1918 virus was reconstituted into infectious particles, which were found to be exceptionally virulent in laboratory tests
   2. While lab mice normally survive infection by modern human influenza viruses, the reconstituted 1918 strain killed 100% of the infected mice & produced enormous numbers of viral particles in their lungs
   3. Due to potential public health risk, publication of full 1918 virus sequence & its reconstitution went forward only after approval by governmental safety panels & ……
      a. After it was also demonstrated that existing influenza vaccines & drugs protected mice from the reconstituted virus

IV. Two basic types of viral infection – lytic & provirus infection
A. Lytic infection - virus usually arrests the normal host synthetic activities & redirects cell to make new viral nucleic acids & proteins that self-assemble into new virions using its available materials
   1. Viruses do not grow like cells; they are assembled from components directly into mature-sized virions
   2. Infected cell eventually ruptures (**lyses**) to release new generation of viral particles & infect neighboring cells
B. Provirus formation – in other cases, infecting virus does not lead to death of host cell, but instead inserts (**integrates**) its DNA into the DNA of host cell's chromosomes; integrated viral DNA is called **provirus**

V. Integrated provirus can have different effects depending on type of virus & host cell - up to 1% of human DNA is DNA from proviruses that infected our ancestors (now just genetic garbage transmitted passively)
A. Bacterial cells containing provirus behave normally until exposed to a stimulus, like UV light
   1. It activates the dormant viral DNA, leading to cell lysis & viral progeny release – ex.: bacterial lambda (λ) virus
B. Some animal cells containing a provirus produce new viral progeny that bud off of cell surface without lysing the infected cell (ex.: HIV); cells may stay alive for a while as a factory that makes new virions
C. Some animal cells containing a provirus lose control over their own growth & division & become malignant (tumor viruses)
   1. This phenomenon is readily studied in lab by infecting cultured cells with the appropriate tumor

VI. Viruses have some virtues – viral gene activities mimic those of host genes & viruses have been used in a variety of ways

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A. They have been used as a research tool used to study host DNA replication & gene expression in their much more complex hosts
B. They are now being used as a means to introduce foreign genes into human cells; this is a technique that will likely serve as the basis for the treatment of human diseases by gene therapy
C. Insect- & bacteria-killing viruses may play role in war against insect pests & bacterial pathogens
   1. Bacteriophages have been used for decades to treat bacterial infections in eastern Europe & Russia, while physicians in the West have relied on on antibiotics
   2. Given the rise in antibiotic-resistant bacteria, bacteriophages may be making a comeback on the heels of promising studies in infected mice
   3. Several biotechnology companies are now producing bacteriophages intended to combat bacterial infections & to protect certain foods from bacterial contamination

VII. T. O. Diener, U. S. Dept. of Agriculture (1971) - discovered an agent causing potato spindle-tuber disease; potatoes get gnarled, cracked; viruses are not the simplest types of infective agents
A. Infectious agent consisted of a small circular RNA totally lacking a protein coat (called pathogen a **viroid**)
B. Viroid traits
   1. Viroid RNAs range from about ~240 to 600 nucleotides (10% the size of the smaller viruses)
   2. No evidence has been found that viroid RNA encodes any proteins; rather, any biochemical activities in which viroids engage take place using host-cell proteins
   3. For example, duplication of viroid RNA in an infected cell uses the host's RNA polymerase II, which normally transcribes host DNA into messenger RNAs
C. Viroids are thought to cause disease by interfering with the cell's normal path of gene expression (e.g., they monopolize RNA polymerase II to duplicate viroid RNA)
D. Viroid diseases can have serious effects on crops
   1. Viroid disease cadang-cadang – has devastated coconut palm groves of the Philippines
   2. Another viroid has wreaked havoc on the chrysanthemum industry in U. S.

# THE HUMAN PERSPECTIVE: THE PROSPECT OF CELL REPLACEMENT THERAPY (1.6)

## Introduction to Cell Replacement Therapy

I. Many human diseases result from the deaths of specific types of cells
A. Type I diabetes results from the destruction of pancreatic beta (β) cells
B. Parkinson's disease occurs with the loss of dopamine-producing neurons in the brain
C. Heart failure can be traced to the death of cardiac muscle cells (cardiomyocytes) in the heart

II. If we could isolate cells from a patient, convert them into the cells that are needed by that patient & then infuse them back into the patient to restore the body's lost function
A. Recent studies have given hope that one day this type of therapy will be commonplace
B. An example is bone marrow transplantation, which is a procedure used widely in current practice; cells are extracted from the interior of the pelvic bones of a donor & infused into the body of a recipient

III. Bone marrow transplantation – used most often to treat lymphomas & leukemias (cancers affecting the number & nature of white blood cells)
A. Patient is exposed to a high level of radiation and/or toxic chemicals, which kills the cancerous cells but also kills all of the cells involved in the formation of red & white blood cells

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1. This treatment has this effect because blood-forming cells are particularly sensitive to radiation & toxic chemicals

B. Once a person's blood-forming cells have been destroyed, they are replaced by transplantation of bone marrow cells from a healthy donor
   1. Bone marrow can regenerate transplant recipient's blood tissue since it contains a small percentage of cells that can proliferate & restock the patient's blood-forming bone marrow tissue
      a. Bone marrow transplantation can be contrasted to simple blood transfusion where recipient receives differentiated blood cells (especially red blood cells & platelets) present in the circulation
   2. These blood-forming cells in the bone marrow are referred to as hematopoietic stem cells (HSCs) & they were discovered in the early 1960s by Ernest McCulloch & James Till (Univ. of Toronto)
      a. HSCs are normally responsible for replacing the millions of red & white blood cells that age & die every minute in our bodies
      b. A single HSC is capable of reconstituting the entire hematopoietic (blood-forming) system of an irradiated mouse

C. A rising number of parents are saving umbilical cord blood of their newborn baby as a type of "stem cell insurance policy" in case the child develops a disease that might be treated by HSC administration

## Potential Cell Replacement Therapy – Adult Stem Cells

I. **Stem cells** are defined as undifferentiated cells that are capable of self-renewal (production of more cells like themselves) & multipotent (can differentiate into ≥2 mature cell types); HSCs of bone marrow are only 1 type

II. Most, if not all, of the organs in human adult contain stem cells capable of replacing the particular cells of the tissue in which they are found
   A. Even the adult brain, which is not known for its ability to regenerate, contains stem cells that can generate new neurons & glial cells (the supportive cells of the brain)
   B. Stem cells are also present in adult skeletal muscle & are called satellite cells; they are thought to divide & differentiate as needed for the repair of injured muscle tissue
   C. Adipose (fat) cells differentiate *in vitro* from adult stem cells that are present within fat tissue
   D. The adult human heart contains stem cells that are capable of differentiating into the cells that form both the muscle tissue of the heart (cardiomyocytes of the myocardium) & the heart's blood vessels
      1. It had been hoped that these cardiac stem cells might have the potential to regenerate healthy heart tissue in a patient who had experienced a serious heart attack
      2. This hope has apparently been realized based on the 2 landmark reports in late 2011 on the results of clinical trials of patients that had suffered significant heart-tissue damage after heart attacks
         a. Stem cells were harvested from each of the patients during heart surgeries, expanded in number through *in vitro* culture, & then infused back into each patient's heart
         b. Over the next few months, a majority of treated patients experienced significant replacement (e.g., 50%) of the damaged heart muscle by healthy tissue derived from the infused stem cells
         c. The regeneration of heart tissue was accompanied by a clear improvement in quality of life compared to patients in the placebo group that did not receive stem cells

III. Adult stem cells are an ideal system for cell replacement therapies since they represent an **autologous** treatment; the cells are taken from the same patient in which they are used; there is no prospect of immune rejection
   A. The dramatic results with cardiac stem cells rekindled interest in adult stem cells, which had waned after a number of failed attempts to direct stem cells isolated from bone marrow to regenerate diseased tissues
   B. The great majority of adult stem cell therapies under development use a type of adult stem cell known as a mesenchymal stem cell (MSC)
      1. These can be obtained from bone marrow, but they are different from the HSCs in that they do not produce blood cells, but rather a variety of other cell types found in various tissues & organs
      2. MSCs can also be obtained from fat tissue obtained during liposuction procedures

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3. Currently, there are well over 100 controlled clinical studies under way for treating a wide range of diseases with MSC-derived cells, like heart disease, diabetes & immune diseases (lupus, Crohn's disease)
4. An MSC-based therapy ("Prochymal") became the first FDA-approved stem cell therapy; it is used to treat Crohn's disease as well as immune reactions that can occur in bone marrow transplant patients

## Potential Cell Replacement Therapy – Embryonic Stem Cells

I. Embryonic stem (ES) cells – very controversial; source of great excitement in field of cell transplantation over the last 1 or 2 decades & also the most heated debates
   A. ES cells are a type of stem cell isolated from very young mammalian embryos; they are cells from the early embryo that give rise to all of the various structures in the mammalian fetus
      1. Unlike adult stem cells, ES cells are **pluripotent**; they are capable of differentiating into every type of cell in the body
         a. ES cells can be cultured indefinitely & there is no controversy over their differentiation capacity
      2. In most cases, human ES cells have been isolated from embryos provided by *in vitro* fertilization clinics
      3. Worldwide, dozens of genetically distinct human ES cell lines, each derived from a single embryo, are available for experimental investigation
   B. Long-range goal of clinical researchers is to learn how to get ES cells to differentiate in culture into each of the many cell types that can be used for cell replacement therapy – considerable progress has been made
      1. Numerous studies have shown that transplants of differentiated, ES-derived cells can improve the condition of animals with diseased or damaged organs

II. The first trials in humans began in 2009 on patients who had experienced debilitating spinal cord injuries
   A. The trial to treat spinal cord injuries used cells (oligodendrocytes) that produce the myelin sheaths that become wrapped around nerve cells
   B. The oligodendrocytes transplanted into these patients were differentiated from human ES cells that were cultured in a medium containing insulin, thyroid hormone & a combination of certain growth factors
      1. This particular culture protocol had been found to direct the differentiation of ES cells into oligodendrocytes rather than any other cell type
   C. Unfortunately, no significant improvement was reported in the treated patients, & the company conducting the trial decided to cease further involvement in the effort

III. Embryonic stem cell therapy is currently under intense study as a treatment for retinal degeneration diseases like macular degeneration
   A. At the time of this writing, there are 8 government-approved clinical trials using ES cells induced to differentiate into retinal pigmented epithelial cells, a key retinal cell type
   B. This is an attempt to cure different forms of retinal degeneration

IV. The primary risk with the therapeutic use of ES cells is the unnoticed presence of undifferentiated ES cells among the differentiated cell population
   A. Undifferentiated ES cells are capable of forming a type of benign tumor, a teratoma, which may contain a bizarre mass of various differentiated tissues, including hair & teeth
   B. The formation of a teratoma within the central nervous system could have severe consequences
   C. In addition, the culture of ES cells at the present time involves the use of nonhuman biological materials, which also poses potential risks

V. The ES cells used in these early trials were derived from cell lines that had been isolated from human embryos unrelated to the pateints who are being treated
   A. Such cells face the prospect of immunologic rejection by the transplant recipient; it may be possible, however, to "customize" ES cells so that they possess the same genetic makeup of the individual being treated

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B. This may be accomplished at some point by a roundabout procedure called **somatic cell nuclear transfer (SCNT)** that begins with an unfertilized egg (a cell obtained from ovaries of an unrelated woman donor)
   1. The nucleus of the unfertilized would be replaced by the nucleus of a cell from the patient to be treated, which would cause the egg to have the same chromosome composition as the patient
   2. The egg would then be allowed to develop to an early embryonic stage, & the ES cells would be removed, cultured & induced to differentiate into the type of cells needed by the patient

C. Because this procedure involves the formation of a human embryo that is used only as a source of ES cells, there are major ethical questions that must be settled before it could be routinely practiced
   1. In addition, the process of SCNT is so expensive & technically demanding that it is highly improbable that it could ever be practiced as part of any routine medical treatment
   2. It is more likely that, if ES cell-based therapy is ever practiced, it would depend on the use of a bank of hundreds or thousands of different ES cells
      a. Such a bank could contain cells that are close enough as a tissue match to be suitable for use in the majority of patients

## Potential Cell Replacement Therapy – Induced Pluripotent Stem Cells

I. It had long been thought that the process of cell differentiation in mammals was irreversible; once a cell had differentiated, it could never revert to any other cell type
   A. This concept was shattered in 2006 when Shinya Yamanaka & colleagues (Kyoto Univ.) announced a stunning discovery
      1. His lab had succeeded in reprogramming a fully differentiated mouse cell (a type of connective tissue fibroblast) into a pluripotent stem cell
      2. They did this by introducing, into the mouse fibroblast, the genes that encoded 4 key proteins that are characteristic of ES cells; these genes (*Oct4, Sox2, Klf4 & Myc*) are known collectively as OSKM
         a. They are thought to play a key role in maintaining the cells in an undifferentiated state & allowing them to continue to self-renew
         b. The genes were introduced into cultured fibroblasts using gene-carrying viruses, & those rare cells that became reprogrammed were selected from the others in the culture by specialized techniques
         c. They called this new type of cells **induced pluripotent cells (iPS cells)**
         d. They demonstrated that they were indeed pluripotent by injecting them into a mouse blastocyst & finding that they participated in the differentiation of all cells in the body, including eggs & sperm
   B. Within the next year or so, the same reprogramming feat had been accomplished in several labs with human cells
      1. There is now an unlimited supply of pluripotent cells that can be directed to differentiate into various types of body cells using similar protocols to those already developed for ES cells

II. Indeed, iPS cells have already been used to correct certain disease conditions in experimental animals, including sickle cell anemia in mice
   A. Based on the experimental results in animal experiments, attempts to use iPS cells in humans are beginning
   B. The first clinical trial of an iPS-cell-based was begun in 2014
      1. Similar to ongoing embryonic stem cell trials, this trial is testing the use of iPS-cell-derived retinal pigmented epithelial cells to treat macular degeneration
      2. Results are not currently available
   C. The utility of iPS cells may extend far beyond cell replacement therapy
      1. iPS cells have also been prepared from adult cells taken from patients with a multitude of genetic disorders
      2. Researchers are then able to follow the differentiation of these iPS cells in culture into the specialized cell types that are affected by the particular disease
      3. It is hoped that such studies will reveal the mechanisms of disease formation as it unfolds in a culture dish just as it would normally occur in an unobservable way deep within the body

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4. The diseased iPS cells have been called "patients in a Petri dish"

D. Example: iPS cells derived from patients with a heart disorder called long QT syndrome differentiate into cardiac muscle cells that exhibit irregular contractions (beats) in culture
   1. This disease-specific phenotype seen in culture can be corrected by several medicines normally prescribed to treat this disorder
   2. Moreover, when these cardiomyocytes that had differentiated from the diseased iPS cells were exposed to the drug cisapride, the irregularity of their contractions increased
   3. Cisapride is a drug that was used to treat heartburn before it was pulled from the market in the US after it was shown to cause heart arrhythmias in certain patients
   4. Results of this type suggest that differentiated cells derived from diseased iPS cells will serve as valuable targets for screening potential drugs for their effectiveness in halting disease progression

III. Unlike ES cells, the generation of iPS cells does not require the use of an embryo
   A. This feature removes all of the ethical reservations that accompany work with ES cells & also makes it much easier to generate these cells in the lab
   B. However, as research on iPS cells has increased, their therapeutic potential has become less clear
      1. For the first few years, it was thought that iPS cells & ES cells were essentially indistinguishable
   C. Recent studies have shown that iPS cells lack the high quality characteristic of ES cells & that not all iPS cells are the same
      1. For example, iPS cells exhibit certain genomic abnormalities that are not present in ES cells, including the presence of mutations & extra copies of random segments of the genome
      2. In addition, DNA-containing chromatin of iPS cells retains certain traces of the original cells from which they were derived, meaning that they are not completely reprogrammed into ES-like, pluripotent cells
         a. This residual memory of their origin makes it easier to direct iPS cells toward differentiation back into the cells from which they were derived than into other cell types
         b. It may be that these apparent deficiencies in iPS cells will not be a serious impediment in the use of these cells to treat disease that affect adult tissues, but it has raised important questions
   D. There are other issues with iPS cells as well – it will be important to develop efficient cell reprogramming techniques that do not use genome-integrating viruses because such cells could develop into cancers
      1. Progress has been made, but the efficiency of iPS cell formation typically drops when other procedures are used to introduce genes
      2. Like ES cells, undifferentiated iPS cells also give rise to teratomas, so it is essential that only fully differentiated cells are transplanted into human subjects
         a. Also, like ES cells, the iPS cells in current use have the same tissue antigens as donors who originally provided them
         b. Thus, they would stimulate an immune attack if they were to be transplanted into other human recipients
      3. Unlike ES cell formation, however, it will be much easier to generate personalized, tissue-compatible iPS cells, because they can be derived from a simple skin biopsy from each patient
         a. Still, it does take considerable time, expense & technical expertise to generate a population of iPS cells from a specific donor
         b. Thus, if iPS cells are ever developed for widespread therapeutic use, they would likely come from a large cell bank that could provide cells that are close tissue matches to most potential recipients
         c. It may also be possible to remove all of the genes from iPS cells that normally prevent them from being transplanted into random recipients

## Potential Cell Replacement Therapy – Direct Cell Reprogramming

I. In 2008, the field of cellular reprogramming took another unexpected turn with the announcement that one type of differentiated cell had been converted directly into another type of differentiated cell (transdifferentiation)

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A. The acinar cells of the pancreas, which produce enzymes responsible for food digestion in the intestine, were transformed into pancreatic beta cells, which synthesize & secrete the hormone insulin
B. The reprogramming process occurred directly in a few days without the cells passing through an intermediate stem cell state
    1. It occurred while the cells remained in their normal residence within the pancreas of a live mouse
C. The reprogramming was accomplished by injection into the animals of viruses that carried 3 genes known to be important in differentiation of beta cells in the embryo

    1. In this case, the recipients of the injection were diabetic mice, & the transdifferentiation of a significant number of acinar cells into beta cells had a positive result
    2. It allowed the animals to regulate their blood sugar levels with much lower doses of insulin
    3. It is also noteworthy that the adenoviruses used to deliver the genes in the experiment do not become a permanent part of the recipient cell
        a. This removes some of the concerns about using viruses as gene carriers in humans
D. Since the first report, many labs have developed *in vitro* methods to directly convert one type of differentiated cell (typically a fibroblast) into another cell type (a neuron, cardiomyocyte or blood-cell precursor)
    1. The procedure was carried out in culture without passing through a pluripotent intermediate
E. In all of these cases, transdifferentiation occurs when the original cells are forced to express certain genes that play a role in the normal embryonic differentiation of the other cell type
    1. It is too early to know whether this type of direct reprogramming strategy has therapeutic potential
    2. However, it certainly raises the prospect that diseased cells that need to be replaced might be formed directly from other types of cells within the same organ

## EXPERIMENTAL PATHWAYS: THE ORIGIN OF EUKARYOTIC CELLS (1.9)

I. Cells can be conveniently divided into 2 groups: prokaryotic cells & eukaryotic cells; almost from the time this division of cellular life was proposed, biologists have wondered about the origin of the eukaryotic cell

II. What is the origin of the eukaryotic cell? - it is generally, but not universally, agreed that prokaryotic cells:
A. Arose before eukaryotic cells **and**
    1. The above point can be verified directly from the fossil record – prokaryotic cells were present in rocks that are ~2.7 billion years old; roughly 1 billion years before any evidence is seen of eukaryotes
B. Gave rise to eukaryotic cells – follows from the fact that the 2 types of cells have to be related to one another because they share many complex traits
    1. Very similar genetic codes, enzymes, metabolic pathways & plasma membranes that could not have evolved independently in different organisms
C. Essentially, because they gave rise to all modern organisms, most scientists agree that these early prokaryotes must have possessed many of the characteristics that are universal in today's living cells

III. Until about 1970, it was generally believed that eukaryotic cells evolved from prokaryotic cells by a process of gradual evolution in which eukaryotic cell organelles became progressively more complex
A. Acceptance of this concept changed dramatically about that time through the work of Lynn Margulis of Boston University
    1. She resurrected an earlier idea that had been dismissed
    2. This was the idea that certain eukaryotic organelles (most notably mitochondria & chloroplasts) had evolved from smaller prokaryotic cells that had taken up residence in the cytoplasm of the larger host cell
    3. Called it the **endosymbiont theory** because it describes how a single composite cell of greater complexity can evolve from 2 or more separate, simpler cells living in a symbiotic relationship with one another
B. Our earliest prokaryotic ancestors were presumed to have been anaerobic heterotrophic cells

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1. Anaerobic because they derived their energy from food energy without using molecular oxygen ($O_2$)
2. Heterotrophic because they were unable to synthesize organic compounds from inorganic precursors ($CO_2$ & water), but instead had to obtain preformed organic compounds from their environment

C. These prokaryotic ancestors are then thought to have acquired the ability to form internal membrane compartments, allowing formation of a nucleus by containing DNA within an internal membrane
1. This development of internal membranes produced the first organism that would be considered eukaryote-like in terms of having a nuleus or other internal compartments
2. Because this is the first organism that subsequently gave rise to all eukaryotes, it is known as the **first eukaryotic common ancestor (FECA)**
3. Although the presence of internal membranes was once thought to be an exclusively eukaryotic trait, it is now known that some bacteria can, in fact, form extensive complex internal membrane systems
   a. The most dramatic example known to date is the bacterium *Gemmata obscuriglobus*, which forms a variety of complex internal membranes
   b. However, careful 3D reconstructions of *G. obscuriglobus* structure show that these membranes do not form closed compartments like eukaryotic organelles
   c. The key step in producing the FECA thus appears not to be formation of internal membranes per se, but instead further development of these membranes into closed internal compartments
   d. In particular, a key step was formation of a compartment surrounding the DNA to produce a nucleus

IV. Once version of endosymbiotic theory

A. Once the internal membrane system had formed, the next step in the evolution of eukaryotes was when a large, anaerobic, heterotrophic prokaryote (a FECA cell) ingested a small, aerobic prokaryote (step 1)

B. Resisting digestion in the cytoplasm, the small, aerobic prokaryote took up residence as a permanent endosymbiont (step 2)
1. As the host cell reproduced, so did the endosymbiont, so that a colony of these composite cells was produced
2. Over many generations, the endosymbionts lost many of the traits no longer required for survival
3. The once-independent, $O_2$-respiring microbes evolved into precursors of modern-day mitochondria

C. Such cells could have given rise to a cell line that evolved other basic eukaryotic traits, including a system of membrane-bound organelle (ER, Golgi complex, lysosomes) - (step 3)
1. They could also have evolved a complex cytoskeleton including cilia, intron splicing & both mitotic & meiotic cell division
2. These characteristics, which are shared among all existing eukaryotic lineages, are proposed to have arisen by a gradual process of evolution rather than in a single step as might occur with an endosymbiont

D. All eukaryotes alive today descended from a cell that acquired these traits (a heterotrophic eukaryotic cell like a fungal cell or protist); it is therefore known as the **last eukaryotic common ancestor (LECA)** - (step 4)
1. Current evolutinary cell biology research focuses on reconstructing the molecular, structural & functional features of the FECA & LECA by comparing features of existing eukaryotic & prokaryotic lineages
2. The oldest fossils thought to be the remains of eukaryotes date back ~1.8 billion years

E. Margulis proposed that acquiring another endosymbiont (specifically a cyanobacterium) may have converted an early heterotrophic eukaryote into a photosynthetic eukaryote ancestor (green algae, plants) – step 5
1. The acquisition of chloroplasts (roughly1 billion years ago) must have been one of the last steps in the sequence of endosymbioses because these organelles are only present in plants & algae
2. In contrast, all known groups of eukaryotes either possess mitochondria or show definitive evidence that they have evolved from organisms that possessed these organelles
   a. The concept that mitochondria & chloroplasts arose via evolution from symbiotic organisms is now supported by an overwhelming body of evidence

V. Division of living organisms into 2 categories, prokaryotes & eukaryotes, reflects a basic dichotomy in cell structure

A. However, this categorization is not necessarily an accurate phylogenetic distinction, reflecting evolutionary relationships among organisms

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B. How are evolutionary relationships between organisms separated in time by billions of years determined?
   1. Most classical taxonomic schemes for classification are based heavily on anatomic or physiologic characteristics
   2. Modern taxonomic schemes that attempt to classify organisms are based on comparisons of the DNA sequences of living organisms
   3. Differences between organisms in amino acid sequence of protein or nucleotide sequence of nucleic acid are the result of mutations in DNA that have been transmitted to offspring
      a. Mutations can accumulate in given gene at a relatively constant rate over long periods of time
      b. Thus, DNA (or amino acid) sequence comparisons can be used to determine how closely organisms are related to one another
      c. So, two closely-related organisms that only diverged recently from a common ancestor should have fewer sequence differences in particular gene than 2 distantly-related organisms
         (1) Two distantly-related organisms would not have a recent common ancestor
      d. This sequence information is used as an evolutionary clock; researchers can build phylogenetic trees showing proposed pathways by which groups of living organisms may have diverged during evolution

C. Carl Woese et al. (Univ. of Illinois, starting in mid-1970s) – compared RNA nucleotide sequence of small ribosomal subunit (16S rRNA in prokaryotes or 18S rRNA in eukaryotes) in different organisms
   1. This RNA was chosen because it is present in large quantities in all cells, it is easy to purify & it tends to change slowly over long periods of evolutionary time
   2. Thus, it can be used to study relationships of very distantly related organisms
   3. In an early study, Woese et al. analyzed the 16S rRNA present in ribosomes of chloroplasts from *Euglena*, a photosynthetic protist
      a. The sequence of this chloroplast rRNA molecule was much more similar to that of the16S rRNA found in cyanobacteria ribosomes than it was to its counterpart in eukaryotic ribosomes in the cytoplasm
   4. This was strong evidence for the symbiotic origin of chloroplasts from cyanobacteria

D. Woese & George Fox (1977) – compared nucleotide sequence of small-subunit rRNAs purified from 13 different prokaryotic & eukaryotic species; a landmark paper
   1. They found that the sequences clustered into 3 distinct groups; the rRNAs within each group are much more similar to one another than they are to the rRNAs of the other 2 groups
      a. First group – contained only eukaryotes
      b. Second group – contained the typical bacteria (gram-positive, gram-negative, cyanobacteria)
      c. Third group – contained several species of methanogenic (methane-producing) bacteria
   2. They concluded, to their surprise, that methanogenic bacteria "appeared to be no more related to typical bacteria than they are to eukaryotic cytoplasms."
   3. These results suggested that the members of these 3 groups represent 3 distinct evolutionary lines that branched apart from one another at a very early stage in the evolution of cellular organisms
   4. Thus, they were assigned to 3 different kingdoms, which they named the Urkaryotes, Eubacteria & Archaebacteria, a terminology that divided prokaryotes into 2 fundamentally distinct groups

D. Subsequent research supported the concept that prokaryotes could be divided into 2 distantly related lineages & expanded the archaebacteria to include at least 2 other groups, the thermophiles & halophiles
   1. Thermophiles – live in hot springs & ocean vents
   2. Halophiles - live in very salty lakes & seas

E. 1989 – 2 published reports rooted the tree of life & suggested that the archaebacteria were actually more closely related to eukaryotes than they were to eubacteria
   1. Both groups of researchers compared the amino acid sequences of several proteins that were present in a wide variety of different prokaryotes, eukaryotes, mitochondria & chloroplasts
   2. In a later paper, a phylogenetic tree constructed from rRNA sequences came to the same conclusion

VI. Woese et al. proposed a revised taxonomic scheme, which has been widely accepted – the archaebacteria, eubacteria & eukaryotes are assigned to separate domains (Archaea, Bacteria & Eucarya, respectively)

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A. Similar DNA sequence analysis studies have shown that eukaryotes then split into 6 distinct lineages, of which animals, including humans, fall into a group known as "opisthokonts"
B. The first major split in the tree of life produced 2 separate lineages, one leading to Bacteria & the other leading to both the Archaea & the Eucarya
    1. If this view is correct, it means that it was an archaebacterium, not a eubacterium, that took in a symbiont & gave rise to the lineage that led to the first eukaryotic cells
    2. Although the host prokaryote in these symbiotic relationships was presumably an archaebacterium, the symbionts that evolved into mitochondria & chloroplasts were almost certainly eubacteria
    3. This is indicated by the close relationship of mitochondria & chloroplasts with modern members of the eubacteria
C. Until 1995, phylogenetic trees were based primarily on analysis of the 16 – 18S rRNA; by then, phylogenetic comparisons of other genes suggested that this scheme might be oversimplified
    1. From 1995 to 1997, the entire sequences of a number of prokaryotic genomes (both archaebacterial & eubacterial) & that of a eukaryote *Saccharomyces cerevisiae* (yeast) were published
        a. This brought the origin of prokaryotic & eukaryotic cells into sharp focus
        b. Researchers could now compare the sequences of hundreds of genes simultaneously
    2. This analysis raised many puzzling questions & blurred the lines of distinction between the 3 domains
        a. Several archaebacteria genomes showed the presence of a significant number of eubacterial genes
        b. Mostly, archaebacterial genes whose products are involved in informational processes (chromosome structure, transcription, translation, replication) were very different from their eubacterial counterparts
        c. In fact, these gene sequences resembled the corresponding genes in eukaryotic cells & fit in well with the scheme outlining the close relationship between the archaebacteria & eukaryotes
    4. In contrast, many archaebacterial genes that encode metabolic enzymes exhibited an unmistakable eubacterial character
    5. The genomes of eubacterial species also showed evidence of a mixed origin, often containing a significant number of genes that bore an archaebacterial character

VII. Most researchers have held to the 3 domain model & argue that the presence of eubacteria-like genes in archaebacteria & vice versa is the result of the transfer of genes from one species to another
A. This phenomenon is referred to as **horizontal gene transfer (HGT)** & sometimes **lateral gene transfer (LGT)**
B. The original premise for the 3-domain model was that genes are inherited from one's parents, not from one's neighbors
    1. This premise allows an investigator to conclude that 2 species are closely related when they both possess a gene (e.g., the rRNA gene) of similar nucleotide sequence
    2. If, however, cells can pick up genes from other species in their environment, then 2 unrelated species may possess genes of very similar sequence
C. An early measure of the importance of HGT in prokaryotic evolution came from a study comparing the genomes of 2 related eubacteria, *Escherichia* & *Salmonella*
    1. 755 genes or nearly 20% of the *E. coli* genome is derived from "foreign" genes transferred into the *E. coli* genome over the past 100 million years since the time when the 2 species diverged
    2. The 755 genes were acquired as result of ≥234 separate lateral transfers from many different sources
    3. Keep in mind that HGT is responsible for the spread of antibiotic resistance in pathogenic bacteria
D. If genomes are a mosaic composed of genes from diverse sources, how does one choose which genes to use in determining phylogenetic relationships?
    1. In one view, genes involved in informational activities (transcription, translation, replication) are the best subjects for determining phylogenetic relationships
        a. This is so because such genes are less likely to be transferred laterally than genes involved in metabolic reactions
        b. The researchers argue that informational gene products (like rRNAs) are parts of large complexes whose components must interact with many other molecules

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c. It is unlikely that such a foreign gene product could be integrated into existing machinery
2. If informational genes are used for comparison, archaebacteria & eubacteria tend to separate into distinctly different groups & archaebacteria & eukaryotes tend to group together as evolutionary relatives

VIII. Analysis of eukaryotic genomes has produced similar evidence of mixed heritage
A. Yeast genome studies show the unmistakable presence of genes derived from both archaebacteria & eubacteria; informational genes tend to have archaeal character & metabolic genes have eubacterial character
B. There are several possible explanations for mixed eukaryotic genome
1. Eukaryotic cells may have evolved from archaebacterial ancestors & then picked up genes from eubacteria with which they shared environments
2. Some of the genes in the eukaryotic cell nucleus are clearly derived from eubacterial genes that have been transferred from the genome of the symbionts that evolved into mitochondria & chloroplasts
3. Others take a more radical position & propose that the eukaryotic genome was originally derived from the fusion of an archaebacterial & a eubacterial cell followed by the integration of their 2 genomes
C. Given these various routes of gene acquisition, it is evident that no simple phylogenetic tree can represent the evolutionary history of the entire genome of an organism
1. Instead, each gene or group of genes of a particular genome may have its own unique evolutionary tree
2. This can be disconcerting for those seeking to determine the origin of our earliest eukaryotic ancestors

# LECTURE HINTS

## The Discovery of Cells

It is useful to give an historical background to the discipline of Cell Biology at the beginning of the course. It sets the stage for what is to follow. The story of the connection between Hooke and van Leeuwenhoek described by Karp is a good one and should be related. Too often, Hooke's and van Leeuwenhoek's accomplishments are described without any mention of such a connection. It is instructive about the level of communication in science that existed in the 1600s and from which science will continue to benefit today if it is not stifled. It may also be useful to mention the quality of van Leeuwenhoek's single lens microscopes. They were examples of superior craftsmanship capable of 300-fold magnification. They were, however, limited in resolution and, therefore, limited in what discoveries they would allow.

The origin of the Cell Theory is equally valuable. I have found the following quote from E. B. Wilson, which I have used when teaching General Biology to be useful in this lecture as well. Wilson stated, less than 75 years after the Cell Theory became widely accepted, that "Long ago it became evident that the key to every biological problem must finally be sought in the cell; for every living organism is, or at some time, has been a cell."

I usually end this section of my lecture by mentioning the biological disciplines, which have given rise to modern Cell Biology: cytology, biochemistry and genetics. I also stress the importance of molecular techniques and molecular biology to the study of Cell Biology nowadays.

If you wish to recommend some extra reading to your students, suggest that they obtain a book called *The Birth of the Cell* by Henry Harris. It is a history of the early days of cell biology with quotes from Hooke, Leeuwenhoek and others. Another fascinating book is a biography of Robert Hooke written by Lisa Jardine; its title is *The Curious Life of Robert Hooke: The Man Who Measured London.* Hooke was a very interesting character who was an engneer, surveyor architect, and inventor in addition to being the first Curator of Experiments at the Royal Society and being the discoverer of cells. He also, along with Christopher Wren, helped to rebuild London after the Great Fire of 1666. He had a fairly bad temper, which got him into trouble

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with some important figures of his time, foremost among them Sir Isaac Newton. Consequently, he has not become the household word that Newton has.

## Leeuwenhoek and Sperm

Among the cells discovered by Anton van Leeuwenhoek (along with his co-discoverer Stephen Hamm) were sperm. According to The People's Almanac #2, upon the discovery in 1677, Leeuwenhoek described the cells he saw as moving "forward with a snakelike motion of the tail." Given the era in which the observation was made, he felt moved to include a disclaimer in his report stating that he had not obtained the sample by "any sinful contrivance" but that his "observations were made upon the excess with which Nature provided [him] in [his] conjugal relations." Despite this, few scientists at the time made the connection between the cells he had observed and conception. Some felt they were parasites. Later, when the connection had been made, some investigators thought that miniature organisms resided in the sperm head and that they expanded slowly upon entering the female. One investigator claimed to see microscopic roosters and horses in the heads of sperm from roosters and horses, respectively. It was even reported later that a tiny human could be seen in the fetal position in the head of a human sperm. This tiny figure was called an homunculus.

## Basic Properties of Cells

For most students, a restatement of the properties common to all cells is a review. However, experience reveals that such reviews are important. These common features are listed in Karp's text.

## Prokaryotes vs. Eukaryotes

Spend some time on the distinctions between prokaryotes and eukaryotes. Deal with any potential vocabulary problems by defining the roots for prokaryote and eukaryote (*kary* - nucleus, *pro* - before, *eu* - true). Students sometimes have difficulty distinguishing between prokaryotes and eukaryotes. Stress the differences and make sure, as much as possible, that they are understood. It might also be a good idea in this section to summarize briefly the major organelles of both types of cells. It serves as a brief reintroduction to terms that the students will hear later.

## The Sizes of Cells and Their Components

The sizes of cells and their organelles are often hard for students to grasp and a brief review of these units of measure is advisable. I do not require my students to memorize the sizes of these cells and organelles, however. These are facts that can be looked up easily in a number of reference books. As a general rule, I am not a fan of memorization (amino acid R groups, structures, metabolic pathways, etc.) and find it better to emphasize concepts. Of course, in some cases, memorization may be the best strategy, but let the students determine that.

Emphasize the importance of the surface area : volume ratio to cell structure and function. Ask students why cells have limits on their sizes. It is important to involve the students frequently in discussions such as this. It helps to keep the class lively. Give them a number of examples of cells that get around the surface area : volume ratio with shapes that help them accomplish specific tasks: nerve cells in the neck of a giraffe, the brush border in intestinal epithelium, relatively large plant cells and others.

There was a movie that terrified me when I was a child in 1959. It was called *The Angry Red Planet.* It was about humans who went to Mars and were able to return. A number of crew members did not survive the journey. At one point, a giant creature that was part bat, part rat and part spider attacked the crew. The more fear-inducing attacker was, however, a gian amoeba-like creature with an eye. Set aside for a moment that it

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had an eye; I was only 9 at the time. The idea of a giant cell attacking the ship and trying to gobble it up is what frightened me. At the time, I did not know about the surface area to volume ratio problem, which would have convinced me that such a creature could not exist, if I had been able to following the reasoning. Since I was only 9, chances are that would not have helped. I tell my students about the movie in order to illustrate this concept. They are amused, and it does get the point across. Some of them have even told me that they looked the movie up on the Internet and watched it. They did not seem to be as impressed as I was.

### Viruses and Viroids

Briefly describe the different kinds of viruses, emphasizing their similarities and differences while you do. Explain the modes of viral infection and the importance of viruses in health issues although that should be reasonably obvious. I usually do not cover viruses in much detail at this point. If there is time remaining at the end of the semester, it is one of the topics I pursue in greater depth. If the students are interested in the topic, I recommend *The Coming Plague* by Laurie Garrett and *The Hot Zone* by Richard Preston. Preston's book reads like a thriller, although it is a true story. It contains a few simplifications so as not to discourage a wider audience, but it is still worthwhile. Garrett's book is a bit more scholarly and wide-ranging, longer and, in some ways, more frightening. Another book worth reading is *The Great Influenza* by John M. Barry, one of many books that describes the influenza pandemic of 1918.

## CRITICAL THINKING QUESTIONS

1. Schleiden and Schwann have justifiably been remembered for their statement of the cell theory, in which they recognized forst that all organisms are composed of one or more cells and that the cell is the structural unit of life. Why, however, might one consider their ideas about the origin of cells to be less insightful? *Both Schleiden and Schwann agreed that cells could arise from noncellular materials, a concept referred to as spontaneous generation. In this conclusion, they have been proved to be incorrect.* What eventually convinced scientists that Schleiden and Scwann were wrong about their explanation for the origin of cells? *Observations by ther biologists were accepted as demonstrating that cells did not arise by spontaneous generation any more than did organisms. By 1855, Rudolf Virchow, a German pathologist, who had ample opportunity inhis chosen field to observe cells giving rise to other cells, stated and convincingly made the case for the third tenet of the cell theory that cells can arise only by division from a preexisting cell.*

   Learning Objective: LO1.1 List the three tenets of the Cell Theory.
   Section Reference: 1.1

2. A fertilized frog egg is allowed to divide and the two daughter cells are then separated in a way similar to what Driesch did with a sea urchin egg at the two-cell stage. What happens? *Both of the separated cells from this early frog embryo will develop into a complete tadpole. The tadpoles will, however, be smaller than if the two daughter cells had not been separated.*

   Learning Objective: LO1.2 List the fundamental properties shared by all cells, explaining their importance.
   Section Reference: 1.2

3. Wilhelm Roux performed an experiment in which he allowed a frog embryo to divide into two cells. He then killed one of the cells with a hot needle, but did not separate the cell he had killed from the remaining cell. The embryo developed abnormally, leading Roux to conclude that the cells in a developing embryo have their developmental potential restricted at each division, even the first. Driesch and others demonstrated that separation of cells in a number of embryos resulted in the development of two smaller, but normal, embryos. Which of these investigators is most likely to have made a procedural error in his

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experimental design and what was it? *Roux made the mistake. By failing to remove the dead cell from the one he had spared, he caused problems in the further development of the embryo. Had he removed the dead cell, the remaining cell would probably have developed normally.*

Learning Objective: LO1.2 List the fundamental properties shared by all cells, explaining their importance.
Section Reference: 1.2

4. You are observing a cell. Its cell wall is made of a long-chain polysaccharide called peptidoglycan, and it has no membrane-bound organelles. It has the ability to make all but the simplest molecules and can make all of the 20 amino acids. What kind of cell is it? *A bacterium*. If the cell contained pigments capable of photosynthesis, what would it be called? *A cyanobacterium.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference: 1.3 & 1.4

5. Early in the Earth's history, the Earth was hot, lacked free oxygen in the atmosphere and conditions were much harsher and more extreme than they are now. How might this fact explain the habitats typically occupied by the Archaea today? *The Archaea are species of bacteria that live in extremely inhospitable environments; they are often referred to as extremophiles. For example, the methanogens can convert $CO_2$ and $H_2$ gases into methane, the halophiles are bacteria that live in extremely salty environments, the acidophiles thrive in very low pH environments and the thermophiles are able to survive at very high temperatures. These habitats closely resemble the Earth early in its history before oxygen appeared in the atmosphere, and they are relatively anaerobic. Archaea have difficulty surviving in more aerobic environments. Archaea are adapted to the environments in which their ancestors arose and evolved and they occupy those environments in the present day wherever those environments can be found.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference: 1.4

6. If one accepts the suggestion that the Archaea are similar to the prokaryotes from which all eukaryotes are descended, how does one explain the extreme environments in which they live when their descendants thrive in more moderate environments? *The environments in which the Archaea live now more closely resemble the environment in which their ancestors evolved earlier in the Earth's history. Their descendant eukaryotes evolved to survive in the relatively benign environment now extant.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference: 1.4

7. What is a metagenome, how is a metagenome produced and what can one learn from a metagenome? *If one wanted to learn about the diversity of prokaryotes in a particular environment, one could attempt to culture all of the microorganisms in that location. This effort would, however, be extremely costly in materials and time would prove to be largely futile. Alternatively, an investigator could concentrate the cells from a sample taken from that environment, for example, a sample of sea water from that particular location. The investigator could then extract the DNA from the concentrated cells and analyze certain DNA sequences present in the preparation. Despite containing some genes in common, those genes would vary considerably from one species to another; this is the essence of biological evolution. By using techniques that delineate the DNA sequences of a particular gene in a particular environment, one can learn directly about the diversity of species living in that habitat. With the modern sequencing techniques available,*

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*which are very rapid and cost-efficient, virtually all of the genes present in the microbes of a given habitat can be sequenced, yielding a collective genome for that habitat, called a metagenome. Such a metagenome can provide information about the types of proteins these organisms produce and, consequently, about the metabolic activities in which they engage.*

Learning Objective: LO1.4 Explain how study of the metagenome increases our understanding of prokaryotic diversity.
Section Reference: 1.4

8. How can the techniques used to generate a metagenome be used for medical purposes in humans and other organisms? *The molecular strategies that are used to produce metagenomes from various habitats have been used to analyze the diversity of microorganisms that live on or within our bodies, for example, those microbes that live in the intestinal tract, the mouth, the vagina, and the skin. This collection of microbes has been named the human microbiome and research is being carried out at an international level to identify and characterize the organisms on people of different age, diet, geography, and state of health.* What has the study of microbiomes taught researchers about the microbiomes of lean and obese humans? *This research has revealed that lean and obese people have markedly different populations of bacteria in their digestive tracts. Furthermore, as obese people lose weight, their bacterial profile shifts toward that of leaner individuals.*

   Learning Objective: LO1.4 Explain how study of the metagenome increases our understanding of prokaryotic diversity.
   Section Reference: 1.4

9. What determines the pathway by which the fertilized human egg can give rise to cells that result in the formation of the approximately 250 distinct types of specialized cells found in the human body? *The specialized cells of a human body, or for that matter of any multicellular organism, are formed by a process called differentiation. The pathways of differentiation, by which some cells become a digestive gland, while others become part of a skeletal muscle or a bone, etc., depend primarily on the signals each cell receives from the surrounding environment. These signals, in turn, depend on the position of that cell within the embryo.*

   Learning Objective: LO1.5 Explain the importance of cell differentiation within a eukaryotic organism.
   Section Reference: 1.5

10. Given the fact that living organisms are highly diverse and that the results obtained from a particular experimental analysis may depend on the organism being studied, what strategy have cell and molecular biologists employed to understand those basic processes that are shared by most organisms, especially humans? *Cell and molecular biologists have focused considerable research activities on a small number of representative or model organisms. The model organisms that have most often been chosen (*E. coli*, the budding yeast,* Saccharomyces cerevisiae, *the flowering plant*, Arabidopsis thaliana, *the nematode,* Caenorhabditis elegans, *a fruit fly,* Drosophila melanogaster, *and a mouse,* Mus musculus) *have specific advantages that make them particularly useful as research subjects for answering certain types of questions.*

    Learning Objective: LO1.5 Explain the importance of cell differentiation within a eukaryotic organism.
    Section Reference: 1.5

11. Prokaryotic cells are generally smaller than eukaryotic cells and have no membrane-bound organelles, which act to transport some materials around the cell and compartmentalize certain cellular processes. Why do prokaryotic cells not require such membrane-bound organelles? *A cell*

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*depends to a large degree on the random movement of molecules (diffusion). The time required for diffusion is proportional to the square of the distance to be traversed. For example, $O_2$ requires only 100 microseconds to diffuse a distance of 1 mm, but requires $10^6$ times as long to diffuse a distance of 1 µm. As a cell becomes larger and the distance from the surface to the interior becomes greater, the time required for diffusion to move substances in and out of a metabolically active cell becomes prohibitively long. Prokaryotic cells are much smaller than eukaryotic cells, and, consequently, simple diffusion is sufficient to move things around the cell. Special membrane-bound organelles that act to move materials around the cell and compartmentalize certain cell processes are thus not necessary because of the small size of prokaryotes.*

Learning Objective: LO1.7 Explain why cells are so small.
Section Reference: 1.7

12. Why are viruses not considered by most biologists to be living organisms? *Outside of a living cell, the virus exists as a particle, or virion, which is little more than a macromolecular package. Virions are macromolecular aggregates, inanimate particles that by themselves are unable to reproduce, metabolize, or carry on any of the other activities associated with life. For this reason, viruses are not considered to be organisms and are not described as being alive.*

Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
Section Reference: 1.8

13. You are studying a virus. It has an icosahedral protein capsid and is surrounded by a lipid-containing envelope. What kind of organism does the virus infect? *It is a eukaryotic virus, specifically an animal virus. Prokaryotic viruses would not have a lipid envelope. Animal viruses, including the human immunodeficiency virus (HIV) responsible for AIDS, often have their protein capsid surrounded by a lipid-containing outer envelope that is derived from the modified plasma membrane of the host cell as the virus buds from the host-cell surface.*

Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
Section Reference: 1.8

14. A virus infects a cell that has been placed in culture. The cell grows into a clone of cells with no apparent infection. Three months later, the cells are exposed to ultraviolet light. Shortly thereafter, most of the cells lyse and shed large amounts of virus. What kind of infection is this? *A provirus had been formed with the viral genome incorporated into the host cell's genome. The host cell is probably a bacterium. Typically, bacterial cells containing a provirus behave normally until exposed to a stimulus like ultraviolet radiation. The ultraviolet light causes the activation of the viral genome and the subsequent lysis of the cell and release of viral progeny.* What kind of infection results in a loss of growth control at some time after infection? *It is a proviral infection. Some animal cells containing a provirus lose control over their own growth and division and become malignant.*

Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
Section Reference: 1.8

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15. You are studying an infectious agent, the effects of which resemble a virus. You isolate the agent and treat it with an enzyme that degrades proteins, and it is unaffected. However, if treated with RNase, it loses its infectivity. What kind of pathogen is it most likely to be? ? *It is a viroid, which is an infectious agent consisting consisting of a small circular RNA molecule that totally lacks a protein coat. Furthermore, no evidence has been found that the naked viroid RNA encodes any proteins. Rather, any biochemical activities in which viroids engage take place using host-cell proteins. Viroids are thought to cause disease by interfering with the cell's normal path of gene expression.*

    Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
    Section Reference: 1.8

## THE HUMAN PERSPECTIVE QUESTIONS: THE PROSPECT OF CELL REPLACEMENT THERAPY

1. Given what you know about tissue and organ transplantation, what factors presently limit the scope of organ transplantation as a treatment for human disease? *The use of organ transplantation in treating human disease is presently significantly limited by the low availability of donor organs and the high risk of immunologic rejection.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

2. In bone marrow transplantation, what is the usual source of the donor cells? *The usual source of the donor cells for bone marrow transplantation is the interior of the donor's pelvic bones.* For what diseases is bone marrow transplantation most often used? *Bone marrow transplantation is most often used as a treatment for lymphomas and leukemias, which are cancers affecting the nature and number of white blood cells.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

3. Briefly summarize the procedure involved in bone marrow transplantation. *First, the patient is exposed to a high level of radiation and/or toxic chemicals. These treatments kill the cancerous cells and also all of the cells involved in the formation of red and white blood cells. Once the blood-forming cells have been destroyed, they are replaced by the transplantation of bone marrow cells from a healthy donor. A small percentage of cells in the transplanted bone marrow can proliferate and restock the recipient's blood-forming bone marrow tissue.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

4. Why are radiation and toxic chemicals ideal for destroying a recipient's blood cells? *The blood-forming cells are particularly sensitive to radiation and toxic chemicals.*

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Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

5. What is the difference between bone marrow transplantation and blood transfusion? *In blood transfusion, the recipient receives only the differentiated blood cells, especially the red blood cells and platelets present in the circulation. Hematopoietic stem cells are not generally present in the circulation; they are typically found only in the bone marrow.*

   Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
   Section Reference:1.6

6. What is the normal purpose of hematopoietic stem cells in the bone marrow? *They are normally responsible for replacing the millions of red and white blood cells that age and die every minute in our bodies.*

   Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
   Section Reference:1.6

7. What characteristics do adult stem cells possess? *Stem cells are undifferentiated cells that are capable of self-renewal, the production of more cells like themselves, and that are multipotent, which means that they are capable of replacing two or more mature cell types. Adult stem cells are such cells that are found in a fully developed organism that has passed the embryonic stage and on its own.* What are some examples of places where adult stem cells have been found in humans? *The hematopoietic stem cells are an example of adult stem cells, as are cells found in the adult brain, the skeletal muscle, and adipose (fat) tissue, among other tissues.*

   Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
   Section Reference:1.6

8. Why are adult stem cells an ideal system for cell replacement therapies? *Adult stem cells are ideal for cell replacement therapies because they would constitute an autologous treatmet; that is, the cells are taken from the same patient in which they will be used for therapy. As a result, these stem cells do not face the prospect of immune rejection.*

   Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
   Section Reference:1.6

9. A number of stem cells have been shown to possess the capability of giving rise to cells from tissues other than their tissue of origin. What is the likely explanation for this variation in cell differentiation? *These differences in cell fate are likely due to signals that the embryonic cells received during development from the surrounding environment; such signals are primarily responsible for the pathway of differentiation that embryonic cells follow. These signals, in turn, depend on the position of a particular cell within the embryo at particular times. If two cells from the same part of the embryo find themselves at different locations during development, they will receive varying developmental signals and will generally have different differentiation pathways as a result.*

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Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.5 & 1.6

10. Which stem cells are defined as stem cells that are isolated from very young mammalian embryos that give rise to all of the various structures of the mammalian fetus? *Embryonic stem (ES) cells.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

11. What type of adult stem cell is currently being used in the great majority of adult stem cell therapies under development? *A mesenchymal stem cell (MSC).* Where can they be obtained and how do they differ from hematopoietic stem cells (HSCs)? *MSCs can be obtained from bone marrow and from fat tissue during liposuction procedures. They differ from HSCs in that they do not produce blood cells, but rather a variety of other cell types found in various tissues and organs.* For what diseases have treatments using MSC-derived cells currently been tested in clinical trials and/or approved by the FDA? *Among the treatments currently being tested are those for heart disease, diabetes and immune diseases such as Lupus and Crohn's disease, and immune reactions that can occur in patients who receive bone marrow transplants.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

12. A trial was begun in 2009 to determine if embryonic stem cells could be used to treat patients who had experienced debilitating spinal cord injuries. What cells were used in this trial and what structure in the nervous system do they produce? *The trial employed oligodendrocytes, cells that produce the myelin sheaths that become wrapped around nerve cell axons.* What hormones were used in the cultures that were established to convert human embryonic stem cells into the cells used in the trial? *The human embryonic stem cells were cultured in a medium containing insulin, thyroid hormone, and a combination of certain growth factors.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

13. What are glial cells? *Glial cells are the supportive cells of the brain.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

14. What is the primary risk with the therapeutic use of ES cells in cell replacement treatments? *The primary risk of using ES cells in cell replacement therapies is the unnoticed presence of undifferentiated ES cells among the differentiated cell population. Undifferentiated ES cells are capable of forming a type of benign tumor, called a teratoma.* What is unusual about these tumors? *Teratomas may contain a bizarre mass of various differentiated tissues, including hair and teeth.*

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Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

15. In cell replacement therapy, what advantage do adult stem cells have over ES cells? *They can be isolated from the individual who is being treated and will thus not face immunological rejection when used in cell replacement therapy.* What disadvantage do these same cells have relative to ES stem cells? *Adult stem cells do not seem to have an unlimited potential to proliferate as is characteristic of ES cells.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

16. How might ES cells be "customized" so that they possess the same genetic makeup as the individual who is being treated, thus protecting them from attack by the recipient's immune system? *The procedure would begin with an unfertilized egg being removed from the ovary of an unrelated woman donor. The nucleus of this egg could then be removed and replaced by the nucleus of a cell from the patient to be treated. The egg would then have the same chromosome composition as that of the patient and would be allowed to develop to an early embryonic stage. After reaching this stage, the ES cells would be removed, cultured and induced to differentiate into the type of cell required by the patient. The name of this procedure is somatic cell nuclear transfer (SCNT)* What is the major ethical question associated with this procedure and what other disadvantages may be connected with the use of this procedure? *It requires the formation of a human embryo that is used only as a source of ES cells. Many would consider it to be an abortion and would therefore object to the use of the procedure. In addition, the process of SCNT is so expensive and technically demanding that it is highly improbable that it could ever be practiced as part of any routine medical treatment. It is more likely that it would depend on the use of a bank of hundreds or thousands of different ES cells. Such a bank could contain cells that are close enough as a tissue match to be suitable for use in most patients.*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

17. What was the experimental procedure that was used to reprogram a fully differentiated mouse cell like a connective tissue fibroblast into a pluripotent stem cell? *This stunning achievement was accomplished by introducing into a mouse fibroblast the genes that encoded four key proteins that are characteristic of ES cells. These genes (*Oct4, Sox2, Klf4, *and* Myc, *known collectively as OSKM) are thought to play a key role in maintaining the cells in an undifferentiated state and allowing them to continue to self-renew. The genes were introduced into cultured fibroblasts using gene-carrying viruses, and those rare cells that had been reprogrammed were selected from the others by specialized techniques.* What were these new cells with stem cells called? *These new cells were called induced pluripotent cells (iPS cells).*

    Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
    Section Reference:1.6

18. How was it demonstrated that these newly-prepared stem cells, the induced pluripotent cells or iPS cells, were, in fact, pluripotent? *The iPS cells were injected into a mouse blastocyst, and it was found that they participated in the differentiation of all of the cells of the body, including eggs and sperm. Within about a year, the same reprogramming feat had been accomplished in several labs with human cells.*

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Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

19. What use, other than cell replacement therapy, has been made of iPS cells? *iPS cells have also been prepared from adult cells taken from patients with a multitude of genetic disorders. Researchers are then able to follow the differentiation of these iPS cells in culture into the specialized cell types that are affected by the particular disease. It is hoped that such studies will reveal the mechanisms of disease formation as it unfolds in a culture dish just as it would normally occur in an unobservable way deep within the body. Furthermore, iPS cells from patients with such ailments could be cultured in the presence of medicines, and, if the phenotype is corrected by the medicine, that medicine could be tested further as a potential treatment for the condition.. Consequently, it has been suggested that differentiated cells derived from diseased iPS cells will serve as valuable targets for screening potential drugs for their effectiveness in halting disease progression.*

Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

20. What ethical advantage does the use of iPS cells have over the use of ES cells? *Unlike ES cells, the generation of iPS cells does not require the use of an embryo. This feature removes all of the ethical reservations that accompany work with ES cells and also makes it much easier to generate these cells in the lab.* What disadvantages have such iPS cells been shown to have as compared to ES cells? *First, studies have shown that iPS cells lack the high quality characteristic of ES cells and also that all iPS cells are not the same. For example, iPS cells exhibit certain genomic abnormalities that are not seen in ES cells, including the presence of mutations and extra copies of random segments of the genome. In addition, the DNA-containing chromatin of iPS cells retains certain traces of the original cells from which they were derived, which means that they are not completely reprogrammed into ES-like, pluripotent cells. This residual memory of their origin makes it easier to direct iPS cells toward differentiation back into the cells from which they were derived than into other types of cells. It will be important to develop efficient cell reprogramming techniques that do not use genome-integrating viruses because such cells carry the potential of developing into cancers. Like ES cells, undifferentiated iPS cells also give rise to teratomas. Also, like ES cells, the iPS cells in current use have the same tissue antigens as the donors who originally provided them, so they would stimulate an immune attack if they were transplanted into a recipient.*

Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

21. How was the transdifferentiation of pancreatic acinar cells into pancreatic beta cells accomplished? *The feat was accomplished by injection into the animals of viruses that carried three genes known to be important in differentiation of beta cells in the embryo. Pancreatic acinar cells, which produce enzymes responsible for digestion of food in the intestine, were transformed into pancreatic beta cells, which synthesize and secrete the hormone insulin. The reprogramming process occurred directly, in a short time, without the cells passing through an intermediate stem cell state. It also occurred while the cells remained in their normal residence within the pancreas of a live mouse.*

Learning Objective: LO1.6 Explain how various types of stem cells may be useful in combatting human disease.
Section Reference:1.6

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# EXPERIMENTAL PATHWAYS QUESTIONS: THE ORIGIN OF EUKARYOTIC CELLS

1. What is some of the evidence that eukaryotic cells are descended from prokaryotic cells? *Prokaryotic and eukaryotic cells share many complex traits, such as very similar genetic codes, enzymes, metabolic pathways and plasma membranes. These similarities could not have evolved independently in different organisms.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

2. What is meant by the term *endosymbiont*? *An endosymbiont is a combination of two cells living in a symbiotic relationship with one of the cells resident inside the other one.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

3. What do the terms "anaerobic" and "heterotrophic" mean? *The term "anaerobic" refers to organisms that derive their energy from food matter without employing molecular oxygen ($O_2$). The term "heterotrophic" refers to organisms that are unable to synthesize organic compounds from inorganic precursors, such as $CO_2$ and water, but instead have to obtain preformed organic compounds from their environment.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

4. What development in our prokaryotic ancestors is thought to have produced the first organism that would be considered eukaryote-like? *The development that gave rise to the first eukaryote-like organism was the acquisition of the ability to form internal membrane compartments; this development of internal membranes allowed the formation of a nucleus (by containing the DNA within an internal membrane) or other internal compartments.* The organism thus formed would have been the first organism that subsequently gave rise to all eukaryotes. What is that organism called? *It is known as the first eukaryotic common ancestor or FECA.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

5. What type of organisms is presumed to have been our earliest prokaryotic ancestors?
   a. autotrophs
   b. heterotrophs
   c. aerobes
   d. anaerobes
   *e. b and d*

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Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

6. How might the endoplasmic reticulum and the nuclear membrane have arisen in primitive eukaryotic cells? *These intracellular membranes might have been derived from a portion of the cell's outer plasma membrane that became internalized. There are a number of current examples of this, the most dramatic of wish is seen in the bacterium* Gemmata obscuriglobus*, which forms a variety of complex internal membranes. It has been demonstrated that these membranes do not form closed compartments like those seen in eukaryotic organelles. Subsequently, such membranes could have developed further into closed internal compartments, particularly a compartment surrounding the DNA to form a nucleus..*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

7. You are studying an anaerobic, unicellular eukaryote that lacks mitochondria. Strangely, the nuclear DNA of these cells is shown to contain genes that are very closely related to a number of mitochondrial genes. What is a possible explanation for this odd finding? *It is likely that these genes were transferred to the nucleus from mitochondria that were once present in the ancestors of these cells. The data suggest that mitochondria were once present in ancestors of these cells and were lost later during the course of evolution.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

8. Assuming that the first step in the formation of eukaryotes was the internalization of membranes that eventually enclosed organelles like the nucleus, what is supposed to have been the next step on the road to the production of a modern eukaryotic cell? *After the internalization of membranes, the next step in the evolution of modern eukaryotes occurred when a FECA cell ingested a small, aerobic prokaryote which somehow resisted digestion within the cytoplasm and took up residence as a permanent endosymbiont. As the host cell reproduced, so did the endosymbiont, so that a colony of these composite cells was soon produced. Over many generations, endosymbionts lost many of the traits that were no longer required for trial, and the once-independent, oxygen-respiring microbes evolved into the precursors of modern-day mitochondria.*

   Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
   Section Reference:1.9

9. What is thought to be the origin of the basic characteristics of eukaryotic cells that did not arise from symbiotic events as is reputed to have happened with the origins of mitochondria and chloroplasts? These other basic characteristics of eukaryotes would include additional internal membrane-bound organelles (endoplasmic reticulum, Golgi complex, lysosomes), a complex cytoskeleton including cilia, intron splicing and both mitotic and meiotic cell division. *These characteristics, which are shared among all existing eukaryotic lineages, are proposed to have arisen by a gradual process of evolution, rather than in a single step as might occur through the acquisition of an endosymbiont.*

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Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

10. The genes for a particular protein in three organisms are examined for differences in their sequences. The gene for organism A differs from that of organism B at 9 locations and organism C at 14 locations. Organism B and organism C differ at only 5 sites. Which two of the three organisms are likely to be most closely related? *Since differences in genes are thought to accumulate with time, those organisms that have accumulated fewer differences between them would be likely to be most closely related. Therefore, B and C would be most closely related. One might also conclude that organism A could be the ancestor of the other two with B being a closer relative to A than C.*

    Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
    Section Reference:1.9

11. How did sequence analysis of 16S rRNA support the endosymbiont theory? *When the 16S rRNA from the chloroplasts and 18S rRNA from the cytoplasm of* Euglena *were analyzed, the sequences of 16S rRNA from the chloroplasts in* Euglena *were found to be much more similar to the rRNA of cyanobacteria than to the 18S rRNAs found in* Euglena *cytoplasm. This suggests that chloroplasts are more closely related to cyanobacteria than to the* Euglena *within which they are contained. This finding constitutes strong evidence for the symbiotic origin of chloroplasts from cyanobacteria by endosymbiosis.*

    Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
    Section Reference:1.9

12. A later and larger comparison of rRNAs in a number of organisms, including 13 different prokaryotic and eukaryotic species, suggested that the methanogenic bacteria are no more closely related to typical bacteria than they are to eukaryotic cytoplasms. What is the evolutionary significance of this finding? *The investigators concluded that these groups of organisms represent three distinct evolutionary lines that branched apart from one another at a very early stage in the evolution of cellular organisms. Thus, they assigned these organisms to three different kingdoms, which they named the Urkaryotes, Eubacteria and Archaebacteria, a terminology that divided the prokaryotes into two fundamentally distinct groups. Subsequent research led to a revised taxonomic scheme, which has been widely accepted. In this scheme, the archaebacteria, eubacteria and eukaryotes are assigned to separate domains, which are named Archaea, Bacteria and Eucarya, respectively.*

    Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
    Section Reference:1.9

13. According to the most recent phylogenetic tree outlining the relationships between the Bacteria, the Archaea, and the Eucarya, what lineage led from the first living cell to the eukaryotes? *According to currentthinking, the first major evolutionary split in the tree of life occurred when the original organisms on the planet split into the line containing the Bacteria and the line leading to both the Archaea and the Eucarya. This would suggest that it was an archaebacterium, not a eubacterium, that took in a symbiont and gave rise to the lineage that led to the first eukaryotic cells. Although the host prokaryote was presumably an archaebacterium, the symbionts that evolved into mitochondria and chloroplasts were*

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*almost certainly eubacteria/cyanobacteria since mitochondria and chloroplasts are closely related to modern members of this group.*

Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

14. According to one of the tenets of modern biology, all living organisms have evolved from a single, common ancestral cell that lived more than three billion years ago. Because it gave rise to all the living organisms that we know of, what name has been given to this cell? *It has been called the last universal common ancestor (or LUCA).*

Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

15. What is lateral or horizontal gene transfer? *Lateral or horizontal gene transfer is the transfer of genes one species to another.*

Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

16. Why are genes that are involved in informational activities, like transcription, translation and replication, the best subjects for determining phylogenetic relationships? *These genes are less likely to be transferred laterally than genes involved in metabolic reactions. The products of informational genes, e.g., rRNAs, are parts of large complexes whose components must interact with many other molecules. It is unlikely that a foreign gene product could become integrated into the existing machinery. Thus, with these genes, any variations would be more likely to be a result of random mutation, which allows phylogenetic relationships to be determined without the muddying influence that would result from lateral gene transfer. Since such mutations can accumulate in a given gene at a relatively constant rate over long periods of time. Consequently, comparisons of nucleotide sequences can be used to determine how closely organisms are related to one another. This type of information can be used as an "evolutionary clock" and helps researchers to construct phylogenetic trees showing proposed pathways by which different groups of living organisms may have diverged from one another during the course of evolution.*

Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

17. The yeast genome shows the presence of genes derived from both archaebacteria and eubacteria. The "informational genes" tend to have an archaeal character and the "metabolic genes" a eubacterial character. What are some possible explanations for this mixed eukaryotic genome? *Eukaryotic cells may have evolved from archaebacterial ancestors and then picked up genes from eubacteria with which they shared environments. In addition, some of the genes in the nucleus of a eukaryotic cellare clearly derived from eubacterial genes that have been transferred from the genomes of the symbionts that evolved into mitochondria and chloroplasts. Another possibility is that the eukaryote genome was originally derived from the fusion of an archaebacterial and a eubacterial cell followed by the integration of their two genomes.*

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Learning Objective: LO1.9 Explain how Margulis and Woese contributed to our understanding of the origin of complex cells.
Section Reference:1.9

## ART QUESTIONS

1. In Figure 1.4, what is the advantage of having the unequal cell division depicted? *During meiosis, eggs often undergo the unequal division so that the bulk of cytoplasmic material ends up in only one of the four possible cells produced by meiosis. This maximizes the chance of survival once the egg is fertilized and development has begun.*

   Learning Objective: LO1.2 List the fundamental properties shared by all cells, explaining their importance.
   Section Reference:1.2

2. Assume that we have repeated the experiment depicted in Figure 1.12, but that we have treated the cells with a drug that dissociates microtubules. When we expose the cells to the fluorescent antibodies against microtubules, what should we see? *The system of microtubules seen in Figure 1.12 should not be present. There may, however, be a slight green glow visible in the cell that is uniformly distributed.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference:1.3

3. Which of the conjugating bacteria in Figure 1.13 is donating genetic material? *The bacterium in the lower part of the picture is donating the DNA. This bacterium possesses pili, structures needed by the bacterium that donates DNA in a conjugating pair. It is through a pilus that the DNA is donated. The other bacterium at the top of the photo has no pili and, consequently, must be the recipient of the DNA.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference:1.3

4. The caption of Figure 1.15a mentions a hypothesis that suggests that chloroplasts evolved from symbiotic cyanobacteria. Name another organelle that may have originated in a similar way. *Mitochondria may have originated in the same way. They have a double membrane like chloroplasts and are similar in a number of other ways.*

   Learning Objective: LO1.3 Compare and contrast the structure and function of a prokaryotic cell and a eukaryotic cell.
   Section Reference:1.3

5. Which of the model organisms in Figure 1.18 would be best for studying the relationships between individual cells in a developing animal? Support your answer. Caenorhabditis elegans, *which is a nematode, would be the best organism for such a study. It consists of a defined number of cells (about 1000). Each of these cells develops according to a precise pattern of cell divisions. Changes in the pattern of cell divisions are likely to be correlated with developmental anomalies. Furthermore, the animal has a transparent body wall, a short generation time and a facility for genetic analysis. All of these factors would make the study of this animal's development much easier.*

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Learning Objective: LO1.5 Explain the importance of cell differentiation within a eukaryotic organism.
Section Reference:1.5

6. Look at Figure 1.19 and use it and the text to answer the following questions. - What is resolution? *Resolution is the ability to distinguish two separate objects as being separate. The resolution distance is the minimum distance separating two objects that still allows them to be distinguished as separate objects.* What are the limits of resolution of the human eye and the light microscope? *The limit of resolution of the human eye and the light microscope are ~0.1 mm (~100 µm) and ~0.1 µm (~100 nm), respectively.*

   Learning Objective: LO1.7 Explain why cells are so small.
   Section Reference:1.7

7. What chemical reagent was used to remove the protein subunits of the Tobacco Mosaic Virus (TMV) pictured in Figure 1.21b? *Phenol.*

   Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
   Section Reference:1.8

8. What is the genetic material of the virus pictured in Figure 1.22b do? *This is a picture of the HIV virus that causes AIDS. The genetic material of this virus is RNA. The enzyme reverse transcriptase that is also picutred converts the RNA genetic material of the AIDS virus to DNA, allowing its integration into the host cell DNA.*

   Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
   Section Reference:1.8

9. Which virus in Figure 1.22 is most likely to infect a bacterium and how does it accomplish this? *The tail fibers allow virus (c.) to attach to the bacterial cell wall. It then injects its DNA into the bacterium, where it takes over cellular functions and produces new progeny viruses.*

   Learning Objective: LO1.8 Describe the structure of a virus and two mechanisms of viral infection of a host cell.
   Section Reference:1.8

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1. Consider some questions about cell structure or function that you would be interested in answering. Would the data required to answer the question be easier to collect by working on an entire plant or animal or on a population of cultured cells? What might be the advantages and disadvantages of working on a whole organism versus a cell culture?

   **Ans:** The specific answer would depend on the question asked. Advantages of working with a cell culture include the ability to study a single cell type, ease of obtaining large numbers of cells, ability to minimize number of unknown variables by using carefully controlled in vitro conditions. The advantage of using a whole organism is that information obtained is more meaningful in understanding the role of the process in the overall activity of the organism. For example, one might want to study glucose transport across the plasma membrane of cultured liver cells in response to insulin, but the results would not tell you much about the role of this process in maintaining proper blood glucose levels.

   **Difficulty:** Difficult
   **Section Reference:**
   1.2

2. Figure 1.3 shows an intestinal epithelial cell with large numbers of microvilli. What is the advantage to the organism of having these microvilli? What do you expect would happen to an individual that lacked such microvilli as the result of an inherited mutation?

   **Ans:** They greatly increase the surface area/volume ratio of the cell, allowing much greater exchange between the cell and the lumen of the intestine. Would be unable to absorb sufficient nutrients from the lumen to survive.

   **Difficulty:** Medium
   **Section Reference:**
   1.2



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3. The first human cells to be successfully cultured were derived from a malignant tumor. Do you think this simply reflects the availability of cancer cells, or might such cells be better subjects for cell culture? Why?

   **Ans:** Cancer cells grow in a much less controlled manner than normal cells, which is why they continue to proliferate in the body. Cancer cells tend to have fewer requirements for growth and are therefore more readily cultured in diverse media than normal cells. Culturing such cells was a logical first step in the development of culture conditions.

   **Difficulty:** Difficult
   **Section Reference:**
   1.2

4. The drawings of plant and animal cells in Figure 1.8*b,c* include certain structures that are present in plant cells but absent in animal cells. How do you think each of these structures affects the life of the plant?

   **Ans:** A major difference between plant and animal cells is the presence of chloroplasts and their associated light harvesting molecules which allow plants to convert light energy to ATP. Plant cells also typically have large vacuoles that consist of fused membrane bound organelles. In plants, vacuoles are often filled with water and help maintain hydrostatic pressure or turgor.

   **Difficulty:** Difficult
   **Section Reference:**
   1.3



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5. It was noted that cells possess receptors on their surface that allow them to respond to specific stimuli. Many cells in the human body possess receptors that allow them to bind specific hormones that circulate in the blood. Why do you think these hormone receptors are important? What would be the effect on the physiological activities of the body if cells lacked these receptors, or if all cells had the same receptors?
   **Ans:** These receptors mark specific cells as targets for particular hormones. Without such receptors, cells would not be able to bind a specific hormone and thus would not be able to respond to it. If all cells had the same receptors, hormones would not be able to selectively activate specific target cells. All cells would become potential targets.

   **Difficulty:** Easy
   **Section Reference:**
   1.2

6. If you were to argue that viruses are living organisms, what features of viral structure and function might you use in your argument?
   **Ans:** That viruses contain genetic material; that they are capable of producing more of themselves, albeit only inside a host cell; that they contain complex biological macromolecules; that they evolve. These are all important criteria of living organisms.

   **Difficulty:** Difficult
   **Section Reference:**
   1.8

7. If we presume that activities within cells do occur in a manner analogous to that shown in the Rube Goldberg cartoon of Figure 1.7, how would this differ from a human activity, such as building a car on an assembly line or shooting a free throw in a basketball game?
   **Ans:** Activities in cells are not directed by agents with a conscious, purposeful goal. Activities that occur in a cell must be directed and regulated by mechanisms operating within the system.

   **Difficulty:** Difficult
   **Section Reference:**
   1.2



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8. Unlike bacterial cells, the nucleus of a eukaryotic cell is bounded by a double-layered membrane studded by complex pores. How do you think this might affect traffic between the DNA and cytoplasm of a eukaryotic cell compared to that of a prokaryotic cell?
   **Ans:** The nuclear envelope that separates the nucleus and cytoplasm in a eukaryotic cell provides the basis for regulating the movement of substances between the two compartments. The DNA of a bacterial cell is presumably much more accessible to cytoplasmic substances than that of a eukaryotic cell.

   **Difficulty:** Easy
   **Section Reference:**
   1.3

9. Examine the photograph of the ciliated protist in Figure 1.16 and consider some of the activities in which this cell engages that a muscle or nerve cell in your body does not.
   **Ans:** Such as, the capture and uptake of other organisms, the sensing of conditions in the external environment and making the appropriate responses, the ability for locomotion. Most activities of this cell are shared by a muscle or nerve cell.

   **Difficulty:** Difficult
   **Section Reference:**
   1.5

10. Which type of cell would you expect to achieve the largest volume: a highly flattened cell or a spherical cell? Why?
    **Ans:** A highly flattened cell because it will have a much greater surface area/volume ratio.

    **Difficulty:** Medium
    **Section Reference:**
    1.3



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11. Suppose you were a scientist living in the 1890s and were studying a disease of tobacco crops that stunted the growth of the plants and mottled their leaves. You find that the sap from a diseased plant, when added to a healthy plant, is capable of transmitting the disease, to that plant.You examine the sap in the best light microscopes of the period and see no evidence of bacteria. You force the sap through filters whose pores are so small that they retard the passage of the smallest known bacteria, yet the fluid that passes through the filters is still able to transmit the disease. Like Dimitri Ivanovsky, who conducted these experiments more than a hundred years ago, you would probably conclude that the infectious agent was an unknown type of unusually small bacterium.What kinds of experiments might you perform today to test this hypothesis?

    **Ans:** You could examine the filtrate under the electron microscope and determine whether the infectious agent was cellular, i.e., bacterial, or noncellular, i.e., viral. You could try to culture the infective agent. If it was a bacterium, you should be able to culture the agent in the absence of host cells, but not so if it were a virus. You could determine the size of the genome (i.e., the RNA or DNA that constituted its genetic material). If it was cellular, it would be expected to have a much larger genome than if it was viral.

    **Difficulty:** Difficult
    **Section Reference:**
    1.8



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12. Most evolutionary biologists believe that all mitochondria have evolved from a single ancestral mitochondrion and all chloroplasts have evolved from a single ancestral chloroplast.
In other words, the symbiotic event that gave rise to each of these organelles occurred only once. If this is the case, where on the phylogenetic tree of Figure 3, page 27, would you place the acquisition of each of these organelles?
**Ans:** Mitochondria would have been acquired somewhere along the line connecting the branch to Archaea and the line leading to the diplomonads. Chloroplasts would have been acquired along the short line leading to plants (which in this tree also includes green algae).

**Difficulty:** Difficult
**Section Reference:**
1.9

13. Publication of the complete sequence of the 1918 flu virus and reconstitution of active viral particles was met with great controversy. Those who favored publication of the work argued that this type of information can help to better understand the virulence of influenza viruses and help develop better therapeutics against them. Those opposed to its publication argued that the virus could be reconstituted by bioterrorists or that another pandemic could be created by the accidental release of the virus by a careless investigator. What is your opinion on the merits of conducting this type of work?
**Ans:** Answers will vary.

**Difficulty:** Medium
**Section Reference:**
1.8



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