Prokaryotic organisms: viruses and bacteria

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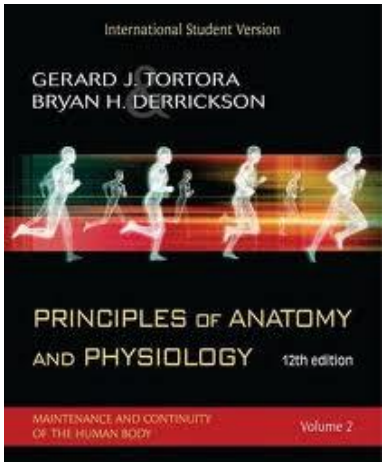
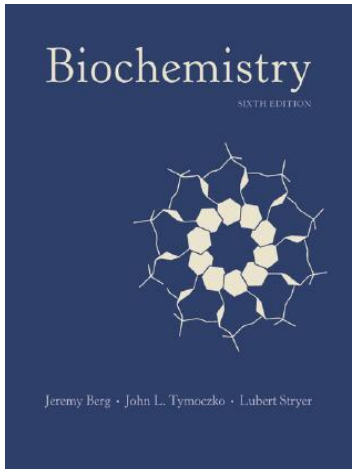
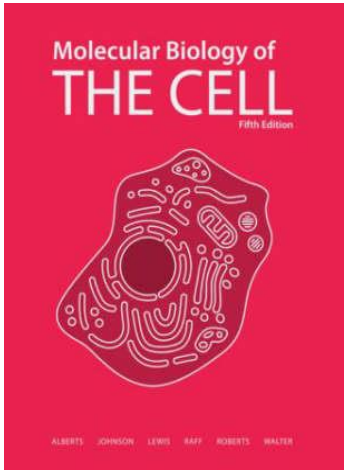
Bibliography

- **Biochemistry by *Jeremy M. Berg***
  - ISBN 10 1429276355
- **Molecular Biology of the Cell 5^{E} by *Bruce Alberts***
  - ISBN10 0815341067
- **Principles of Anatomy and Physiology by *Gerard J. Tortura***
  - ISBN 10 0470233478

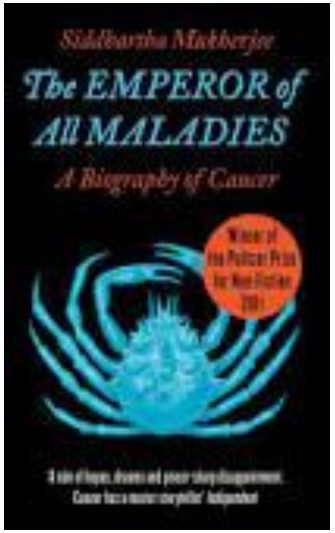


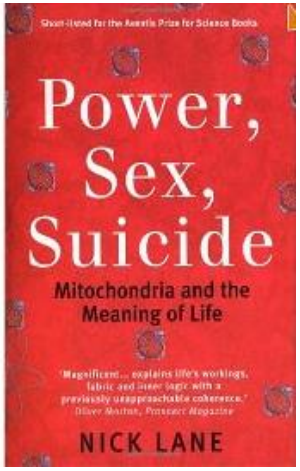


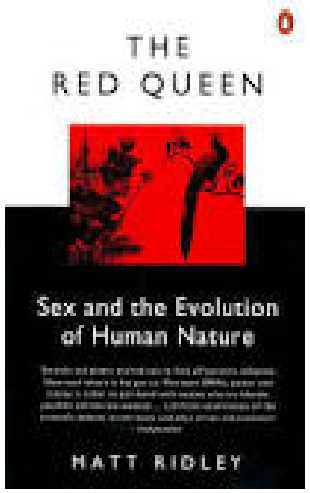


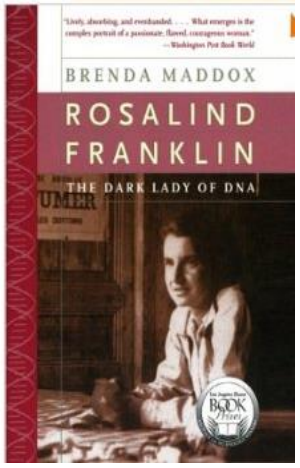
Some light reading

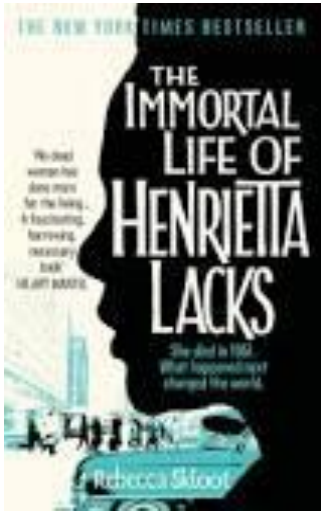
- The emperor of all maladies, *Siddhartha Mukherjee*
- The immortal life of Henrietta Lacks, *Rebecca Skloot*
- The dark lady of DNA, *Brenda Maddox*
- The red queen, *Matt Ridley*
- Power, Sex, Suicide, *Nick Lane*
- The Spark of Life, *Frances Ashcroft*











Today's Lecture

- Introduction to pathogens
- Introduction to prokaryotes - bacteria
- Interactions of bacteria with host cells
- Introduction to viruses
- Introduction to eukaryotic pathogens
- Introduction to prions
- The microbiome

Cellular Microbiology

- **Bacteriology**
  - The study of bacteria
  - Early discipline did not address the aspects of the environment on bacterial 'factors'
  - Absent (unobserved) features of pathogens

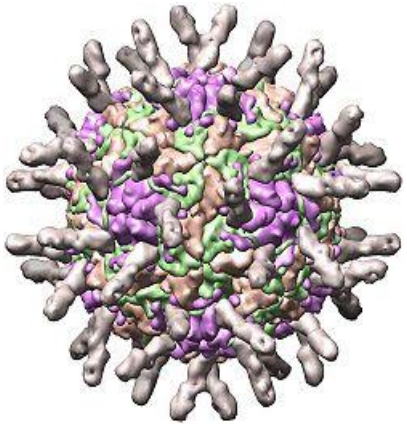
- **The discipline of cellular microbiology addresses host-pathogen interactions to elucidate pathogenesis (the creation of a pathologic condition).**

- **Pathogen: A microorganism that causes disease**
  - Disease: Absence of ease; uneasiness, discomfort; inconvenience, annoyance; disquiet, disturbance; trouble

- **Bacterial pathogens often infect animals and plants**
  - Interact, invade, colonize and infect hosts
    - Culminating in disease (but not always)
    - Aggressive, Opportunistic, Quiescent
      - Infection: The agency, substance, germ, or principle by which (an infectious) disease is communicated or transmitted; morbific influence

What is a pathogen?

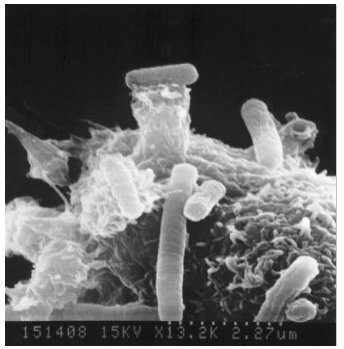
Human Rhinovirus

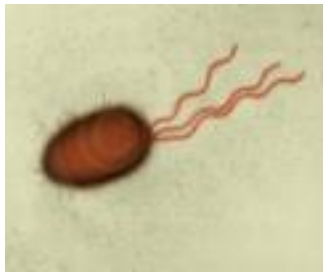


an **infectious** biological agent
that causes disease to its host

Viruses (Flu)
Fungi (Candida)
Bacteria (Tuberculosis)
Protozoa (Cryptosporidium)
Parasites (Malaria)
Prions (Mad cow disease)

Enteric bacteria





Severe diarrhea!!!!

MINES Saint-Étienne

Pathogen types

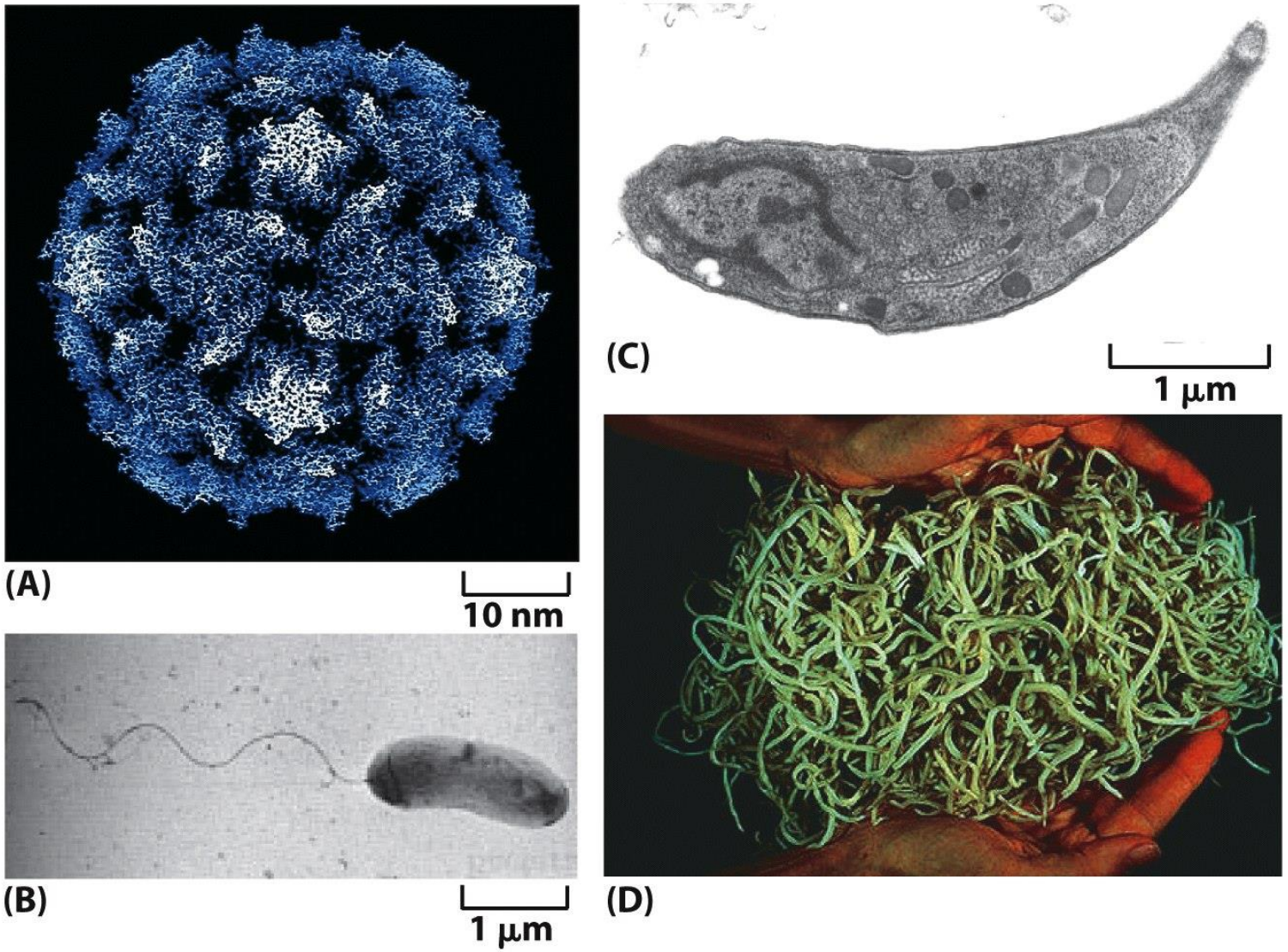


Figure 24-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Why Detect/Study Pathogens?

- Pathogen detection is important for :
- Diagnostics, health of individual and population
- Food safety
- Water safety
- Environmental Pollution (algae, fungi etc.)
- Drug development
- Basic Research

Worldwide mortality due to infectious diseases WHO

Rank	Cause of death	Deaths 2002	Percentage of all deaths	Deaths 1993	1993 Rank
N/A	All infectious diseases	14.7 million	25.9%	16.4 million	32.2%
1	Lower respiratory infections	3.9 million	6.9%	4.1 million	1
2	HIV/AIDS	2.8 million	4.9%	0.7 million	7
3	Diarrheal diseases	1.8 million	3.2%	3.0 million	2
4	Tuberculosis (TB)	1.6 million	2.7%	2.7 million	3
5	Malaria	1.3 million	2.2%	2.0 million	4
6	Measles	0.6 million	1.1%	1.1 million	5
7	Pertussis	0.29 million	0.5%	0.36 million	7
8	Tetanus	0.21 million	0.4%	0.15 million	12
9	Meningitis	0.17 million	0.3%	0.25 million	8
10	Syphilis	0.16 million	0.3%	0.19 million	11
11	Hepatitis B	0.10 million	0.2%	0.93 million	6
12-17	Tropical diseases	0.13 million	0.2%	0.53 million	9, 10, 16-18

Note: Other causes of death include maternal and perinatal conditions (5.2%), nutritional deficiencies (0.9%), noncommunicable conditions (58.8%), and injuries (9.1%).

Human Pathogens of Significance

- **Many… although certain pathogens are still global threats or major etiologic agents of life threatening disease**
  - Pandemic strains (cholera, typhoid)
  - Antibiotic resistance (*endless battle that health professionals are currently losing*)
  - Chronic pathogens associated with genetic disorders
  - Opportunistic pathogens (taking hold with entrance wounds, immune deficiency, age)

Diversity and niches

- **Enterics**
  - Extracelluar, intracellular, invasive, shedding
- **Respiratory**
  - Lung, tracheal, bronchial infections
- **Sepsis**
  - Blood infections (serum resistant!)
- **Skin infections (wounds, cuts)**

What does a pathogen infect?

- Can infect animals, plants, insects, even other bacteria
- Pathogens enter through orifices (nose, mouth, vagina etc.), breaks in skin, eyes, insect bites
- Pathogens infect specific targets in the host
- Usually have a target molecule on the host cell
- Can be intracellular or extracellular
- Not necessarily living organisms

What does a pathogen infect?

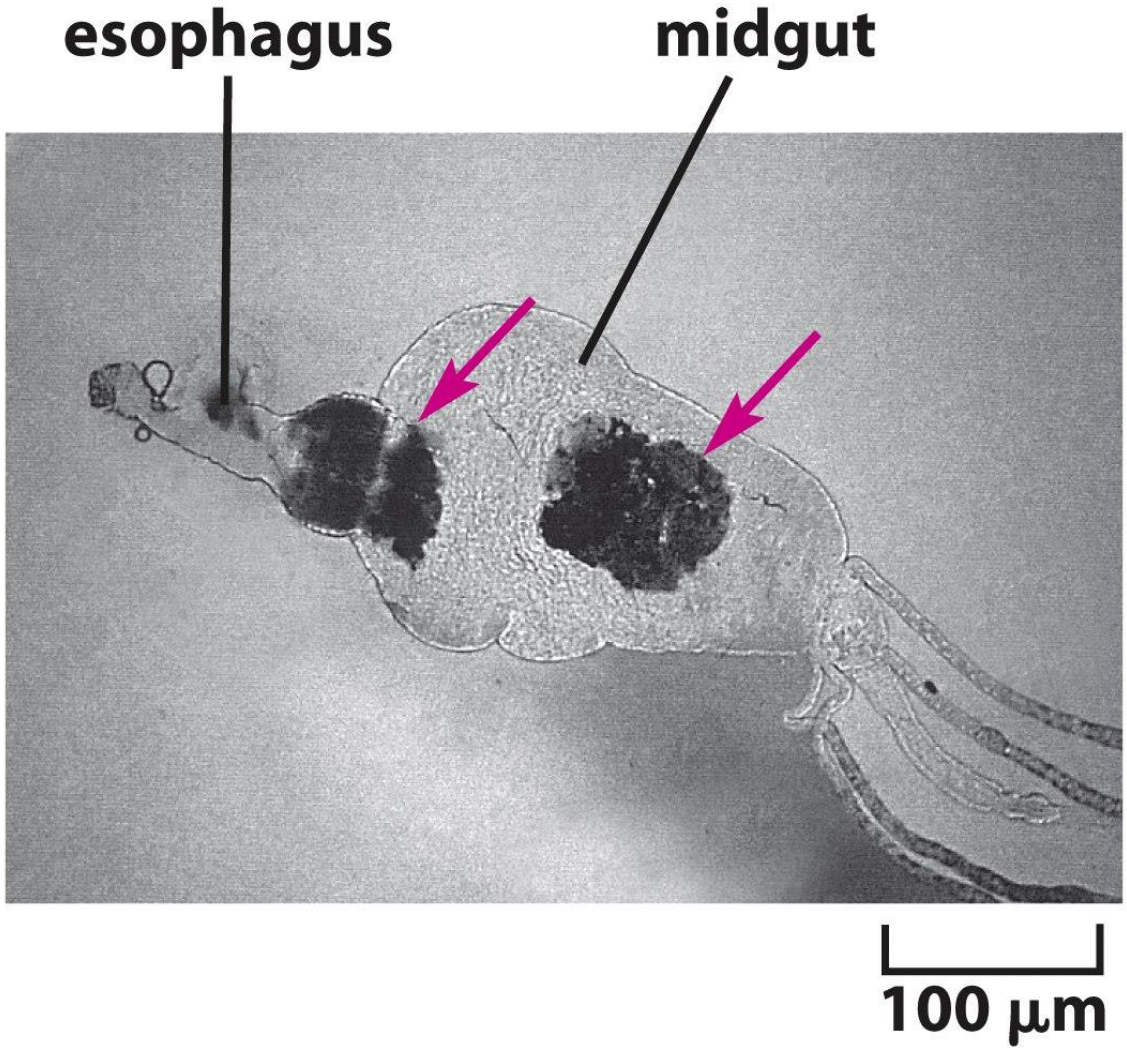
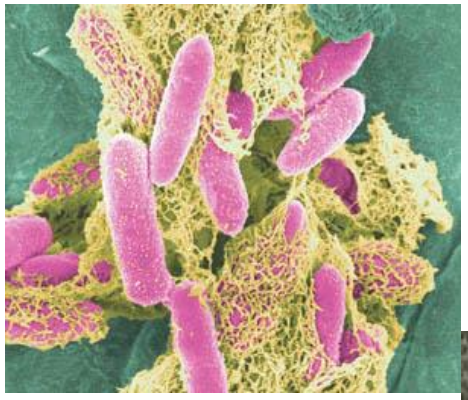


Figure 24-20 *Molecular Biology of the Cell* (© Garland Science 2008)

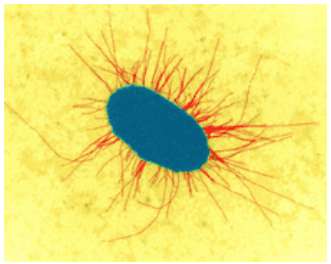
What are bacteria?

- **Single celled organisms**
- **Very small**
- **Need a microscope to see**
- **Can be found on most materials and surfaces**
- **Billions on and in your** body right now



E. Coli O157:H7 can make you very sick.

Streptococcus can cause strep throat.



This *E. coli* helps you digest food.

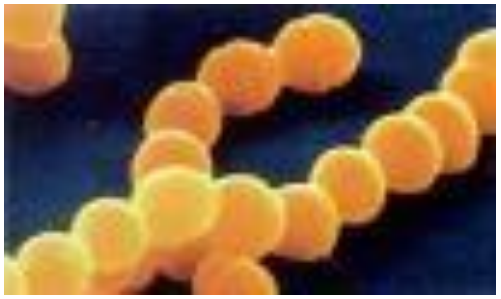
What do they look like?

Three basic shapes

- Rod shaped called bacilli (buh-sill-eye)
- Round shaped called cocci (cox-eye)
- Spiral shaped

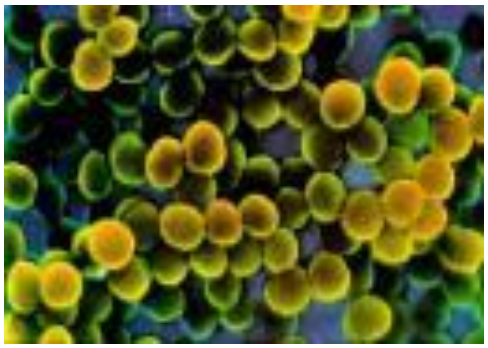
Bacilli

Cocci



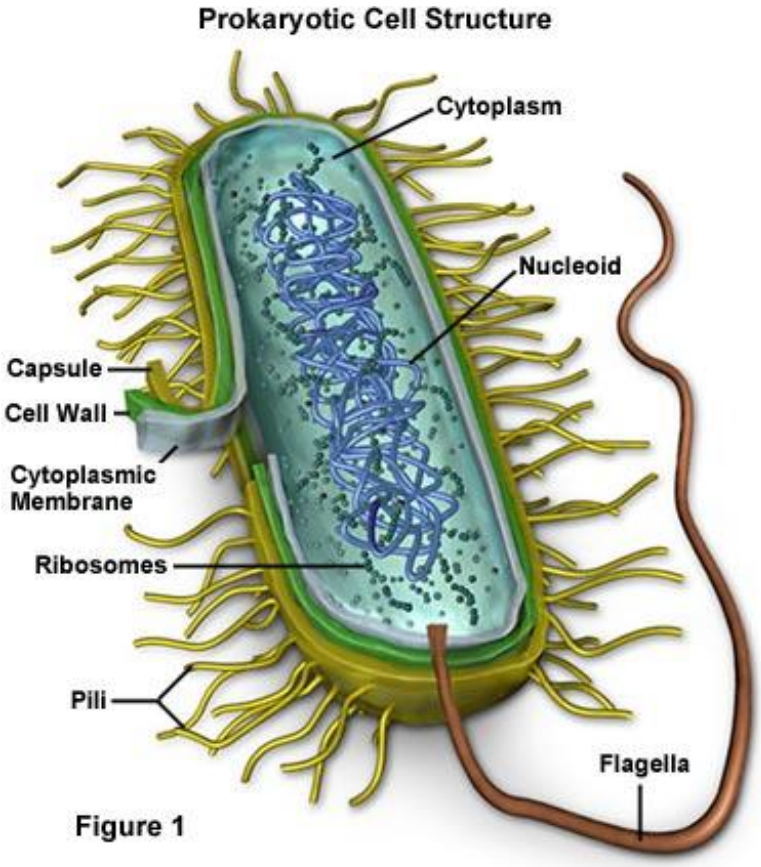
Some exist as single cells, others cluster together

Cluster of cocci



Spiral

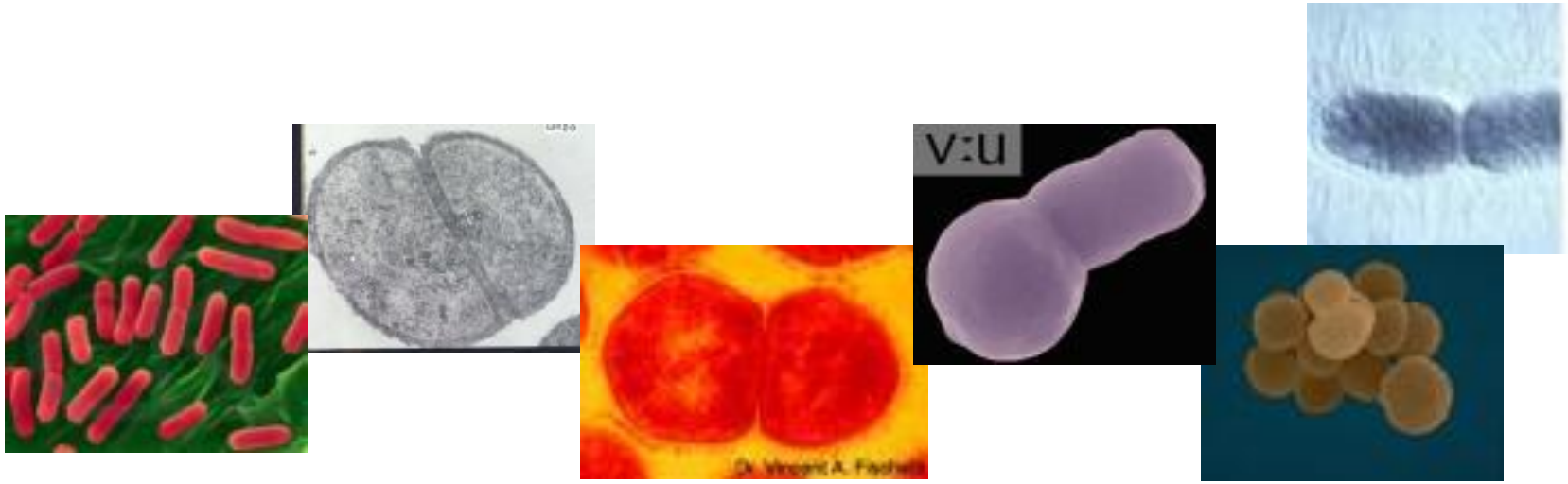
Bacteria are ALIVE!



- **What does it mean to be alive?**
  - They reproduce (make more of themselves)
  - They need to eat

How do bacteria reproduce?

- **Grow in number not in size**
  - Humans grow in size from child to adult
- **Make copies of themselves by dividing in half**
  - Human parents create a child



USDA NIFSI Food Safety in the Classroom©
University of Tennessee, Knoxville 2006

How do bacteria eat?

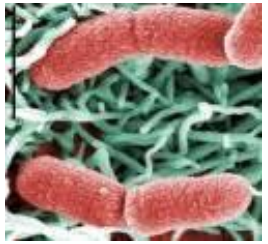
- **Some make their own food from sunlight—like plants**

Photosynthetic bacteria

- **Some are scavengers**
  - Share the environment around them
    - Example: The bacteria in your stomach are now eating what you ate for breakfast

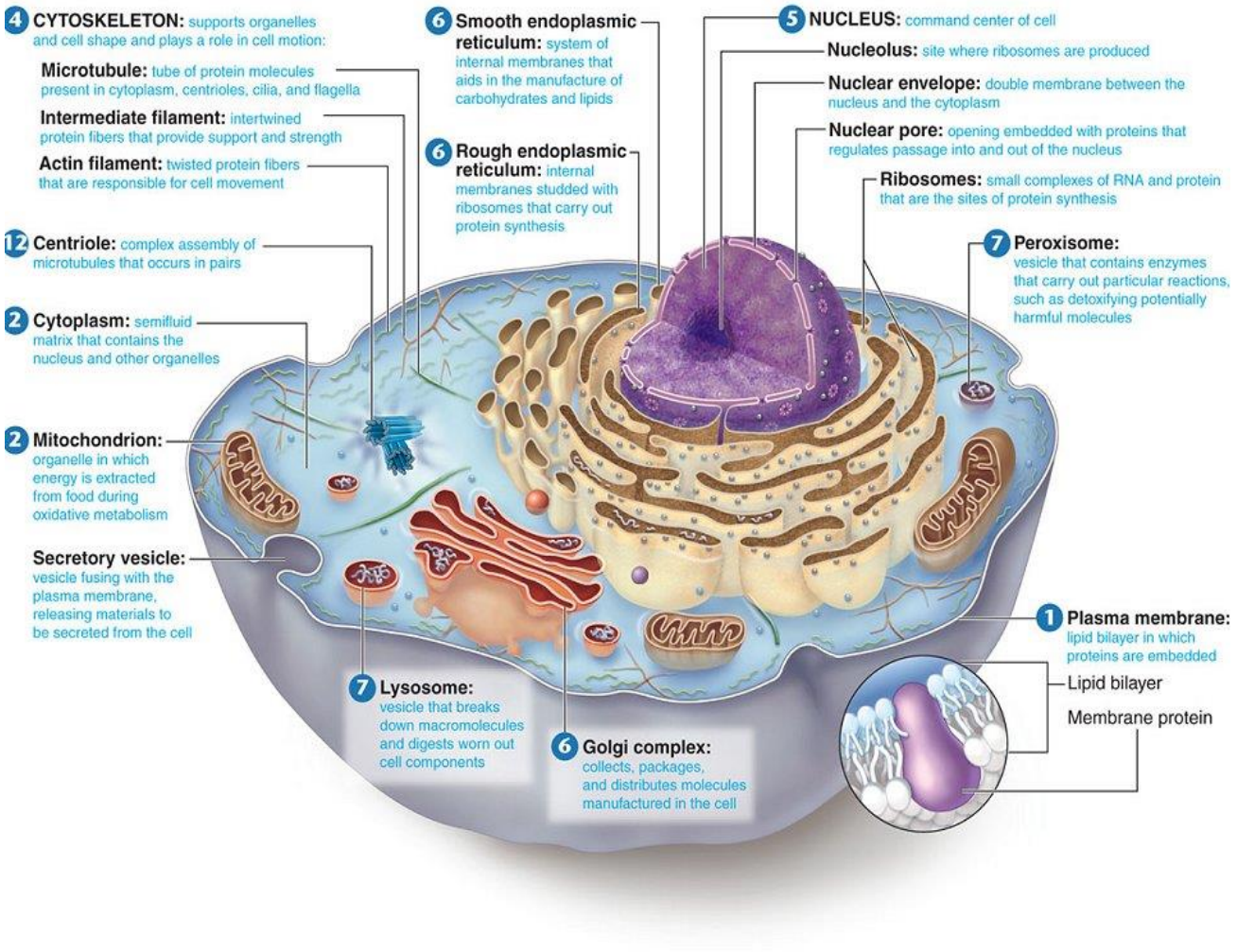
Harmless bacteria on the stomach lining

- **Some are warriors (pathogens)**
  - They attack other living things
    - Example: The bacteria on your face can attack skin causing infection and acne



E. Coli O157:H7 is a pathogen

Review of animal cell structure



stephenyardleybrendan.blogspot.com

Comparison of Eukaryotic and Prokaryotic Cells

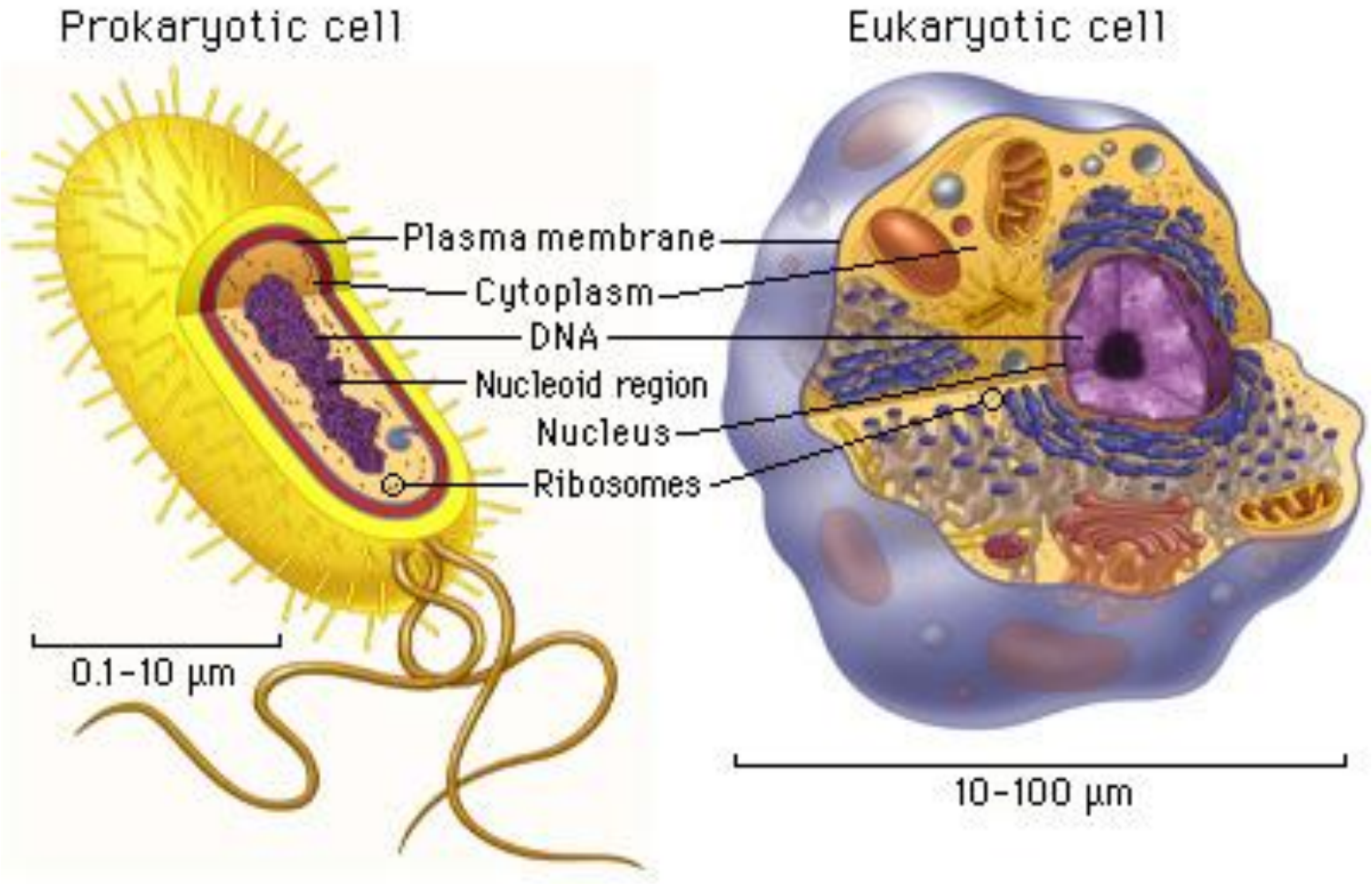
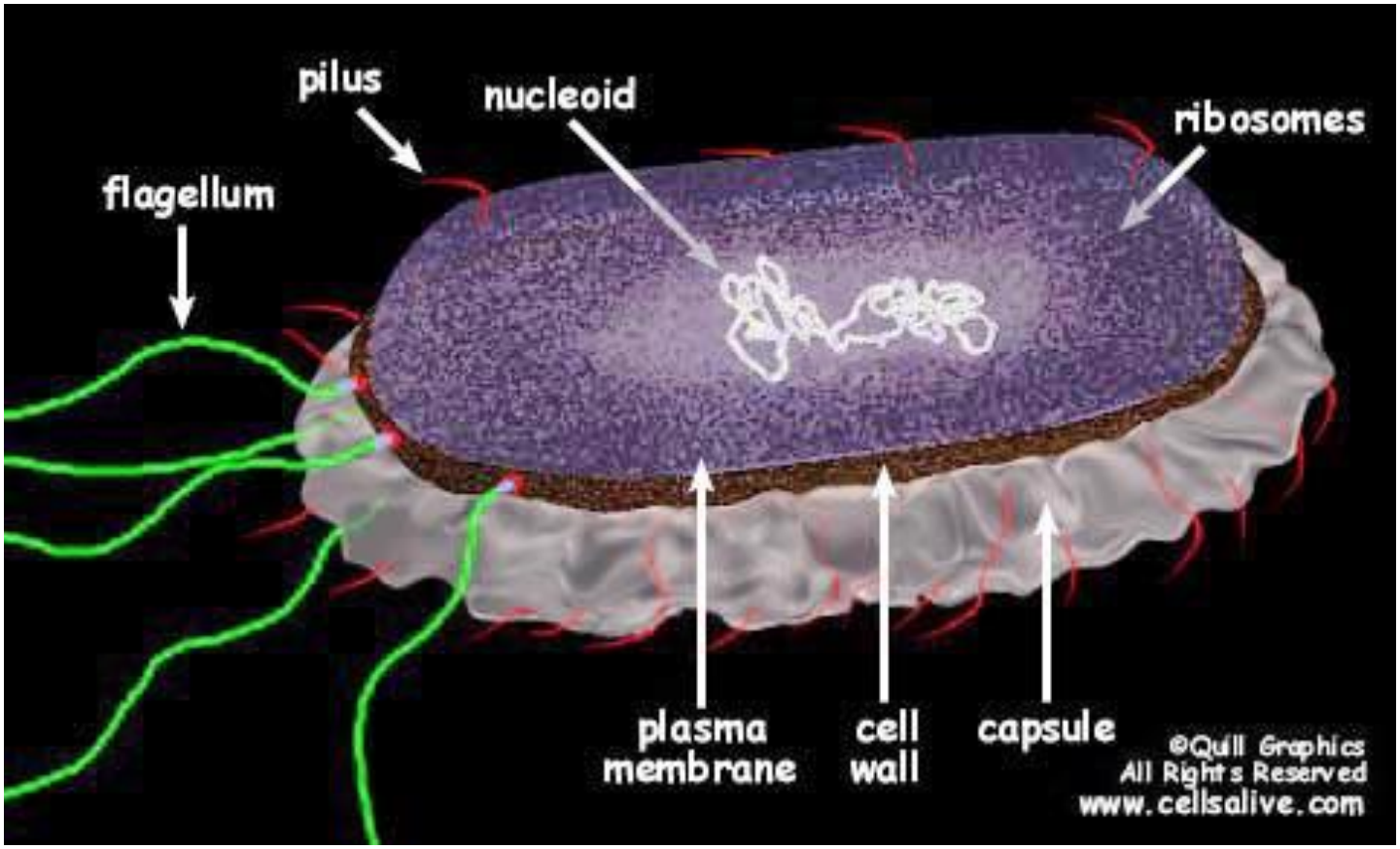


Image: k12station.blogspot.com/2006_08_01_archive.html

Key features of a bacterium

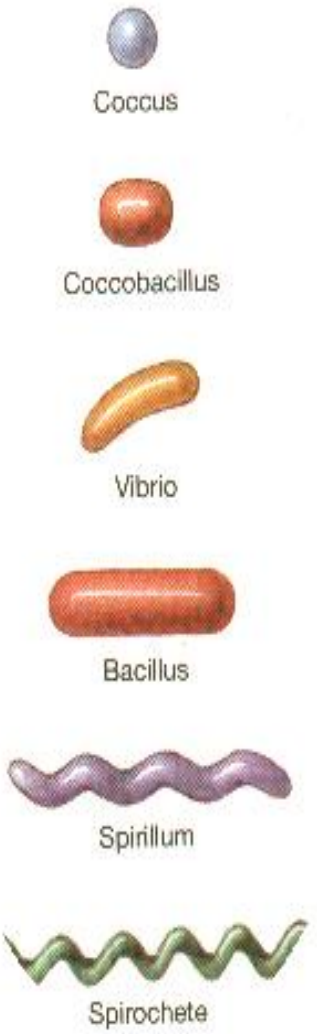


Size of Bacteria

- **Average bacteria 0.5 - 2.0 µm in diam.**
  - RBC is 7.5 µm in diam.
- **Surface Area ~12 µm²**
- **Volume is ~4 µm**
- **Surface Area to Volume is 3:1**
- **Typical Eukaryote Cell SA/Vol is 0.3:1**
- **Food enters through SA, quickly reaches all parts of bacteria**
- **Eukaroytes need structures & organelles**

Shapes of Bacteria

- **Coccus**
  - Chain = Streptoccus
  - Cluster = Staphylococcus
- **Bacillus**
  - Chain = Streptobacillus
- **Coccobacillus**
- **Vibrio = curved**
- **Spirillum**
- **Spirochete**
- **Square**
- **Star**



Shapes of Bacteria

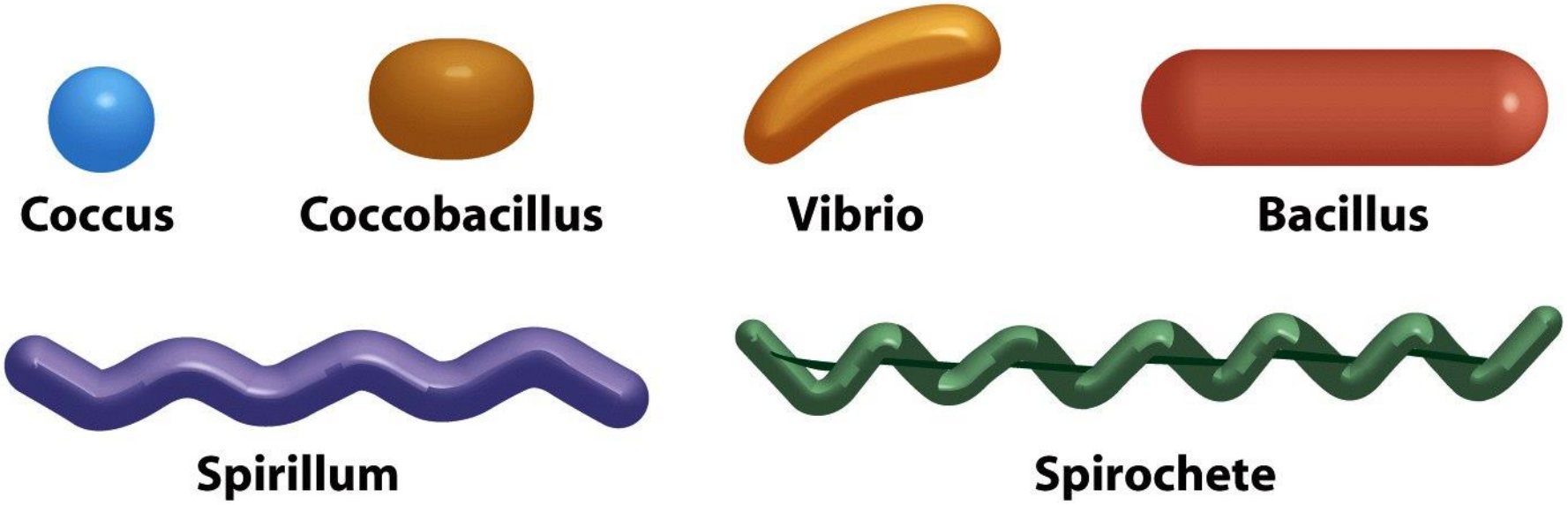
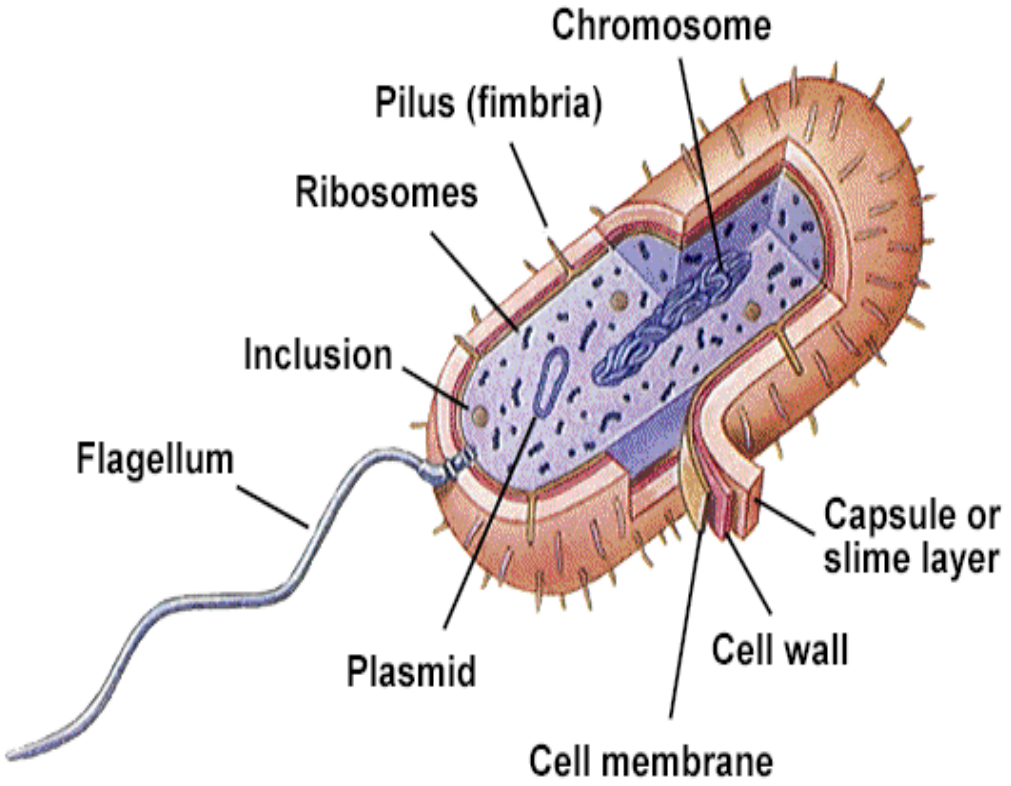


Figure 24-4a *Molecular Biology of the Cell* (© Garland Science 2008)

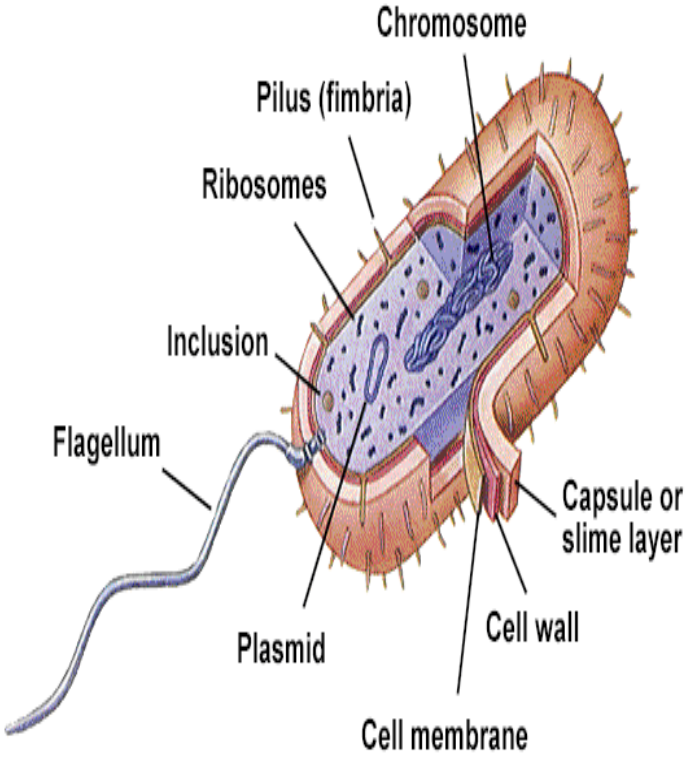
Bacterial Structures

- Flagella
- Pili
- Capsule
- Plasma Membrane
- Cytoplasm
- Cell Wall
- Lipopolysaccharides
- Teichoic Acids
- Inclusions
- Spores



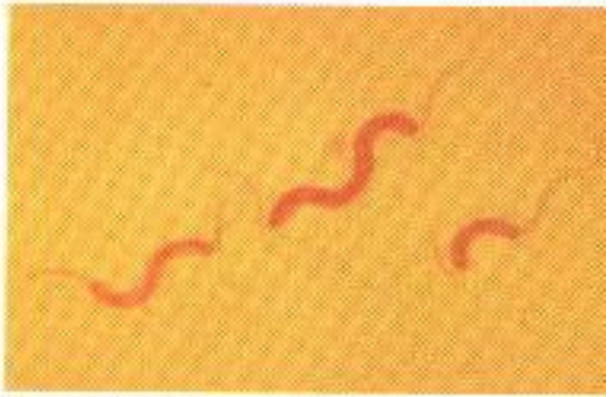
Flagella

- **Motility - movement**
- **Swarming occurs with some bacteria**
  - Spread across Petri Dish
  - Proteus species most evident
- **Arrangement basis for classification**
  - Monotrichous; 1 flagella
  - Lophotrichous; tuft at one end
  - Amphitrichous; both ends
  - Peritrichous; all around bacteria



Flagella

(a)



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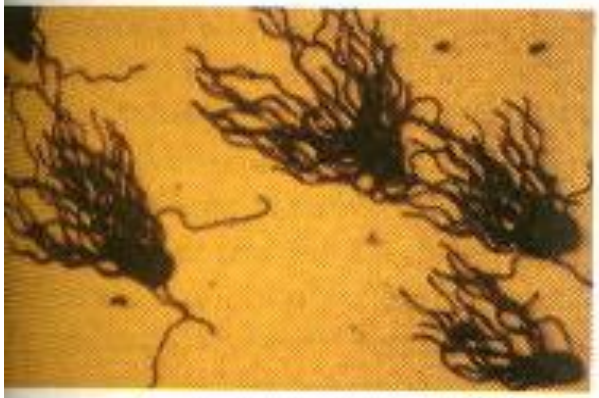
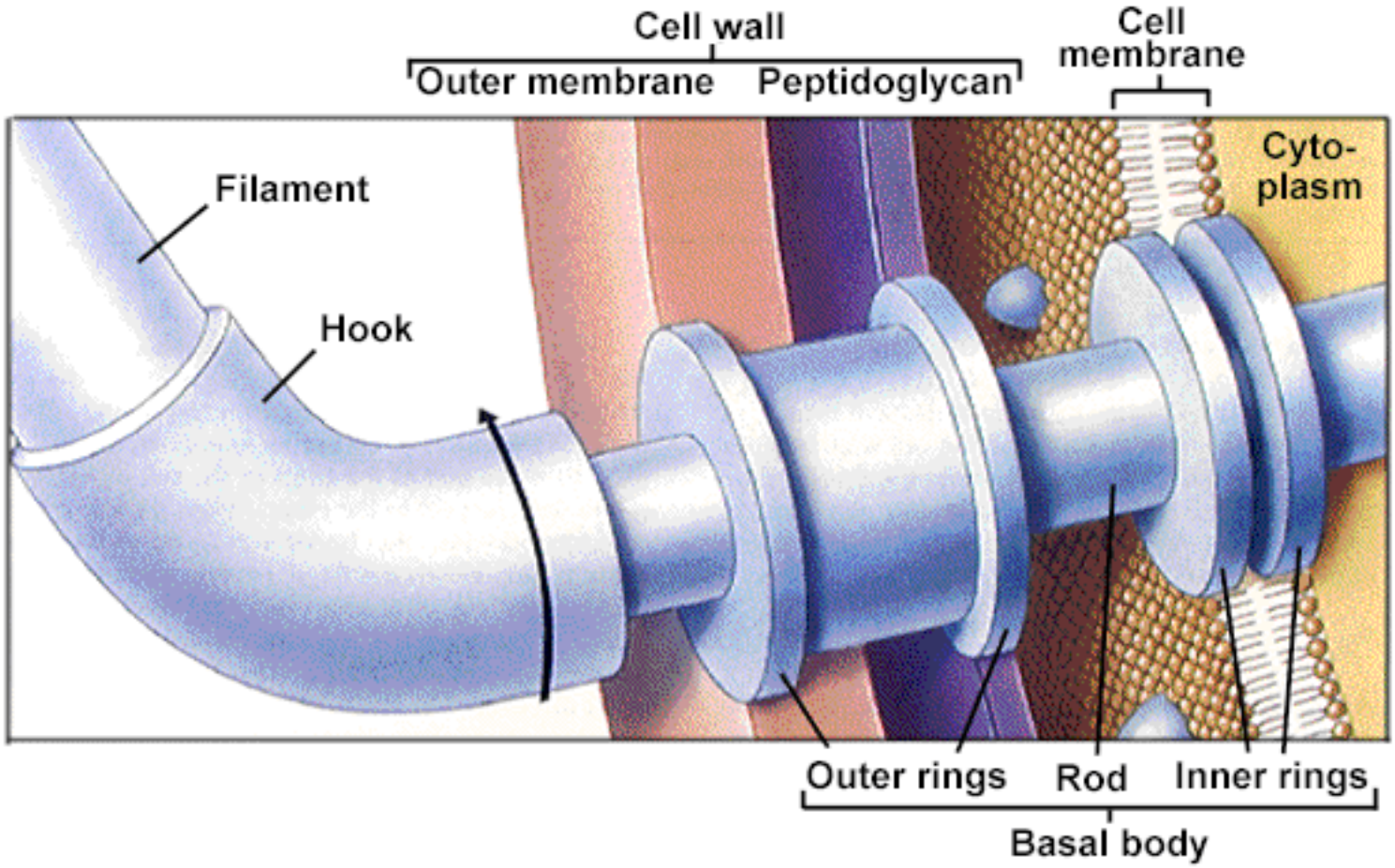


(d)

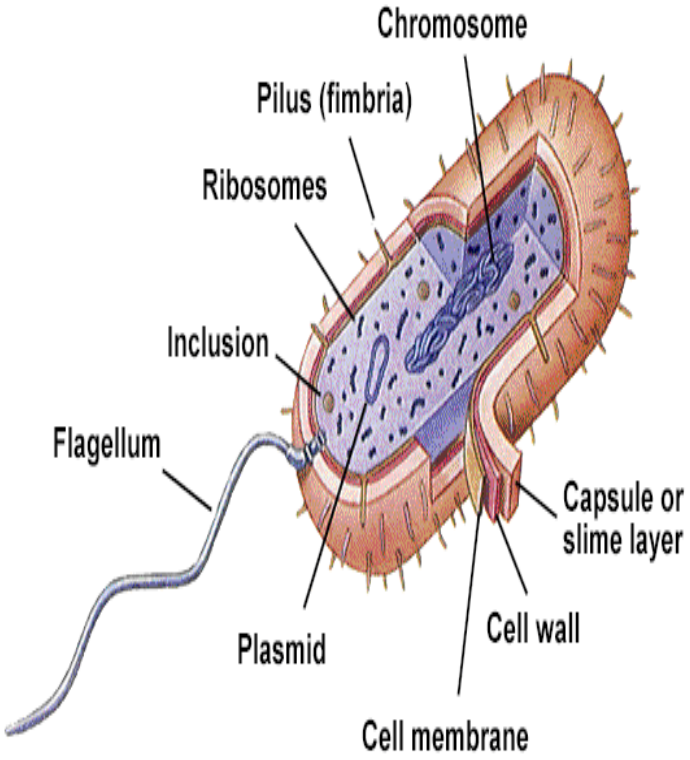
(e)

Flagella


Cell wall
Outer membrane
Peptidoglycan
Cell membrane
Cyto-plasm
Filament
Hook
Outer rings
Rod
Inner rings
Basal body

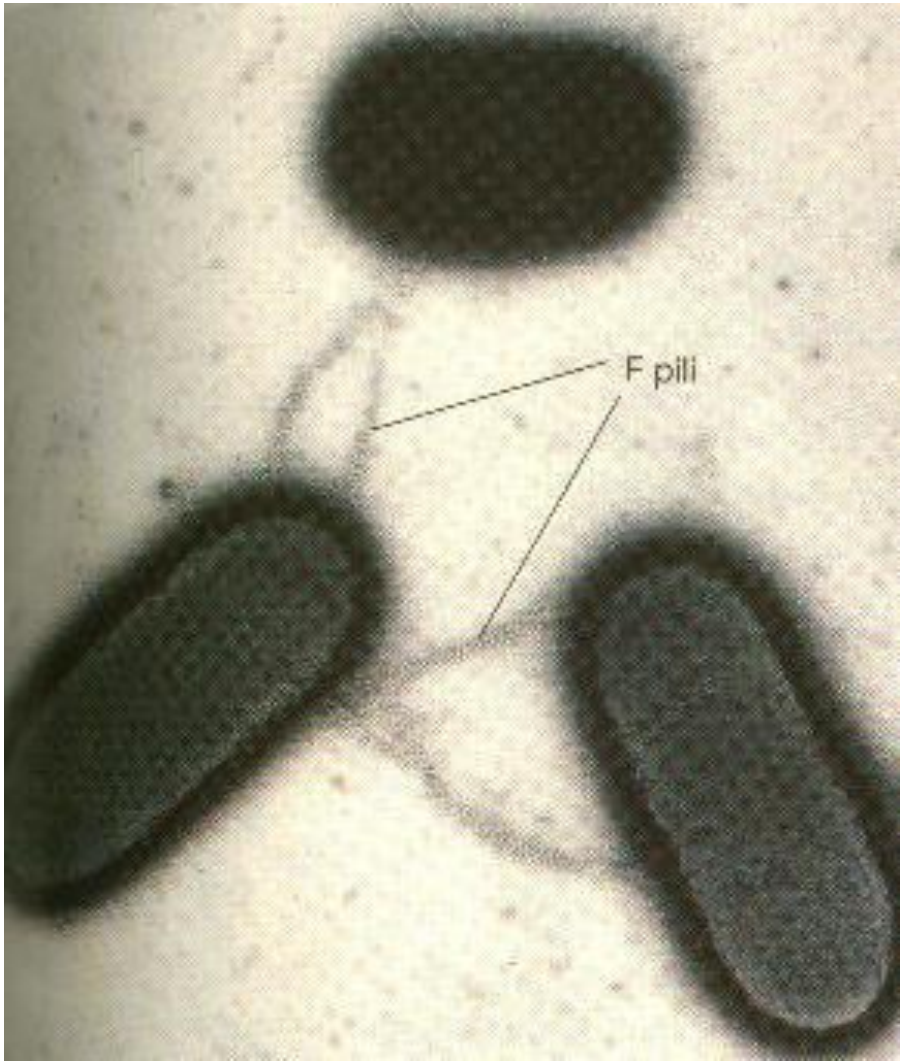
Pili

- **Short protein appendages**
  - smaller than flagella
- **Adhere bacteria to surfaces**
  - *E. coli* has numerous types
    - K88, K99, F41, etc.
  - Antibodies to will block adherence
- **F-pilus; used in conjugation**
  - Exchange of genetic information
- **Flotation; increase buoyancy**
  - Pellicle (scum on water)
  - More oxygen on surface



F-Pilus for Conjugation

F-Pili



Flagella vs pili

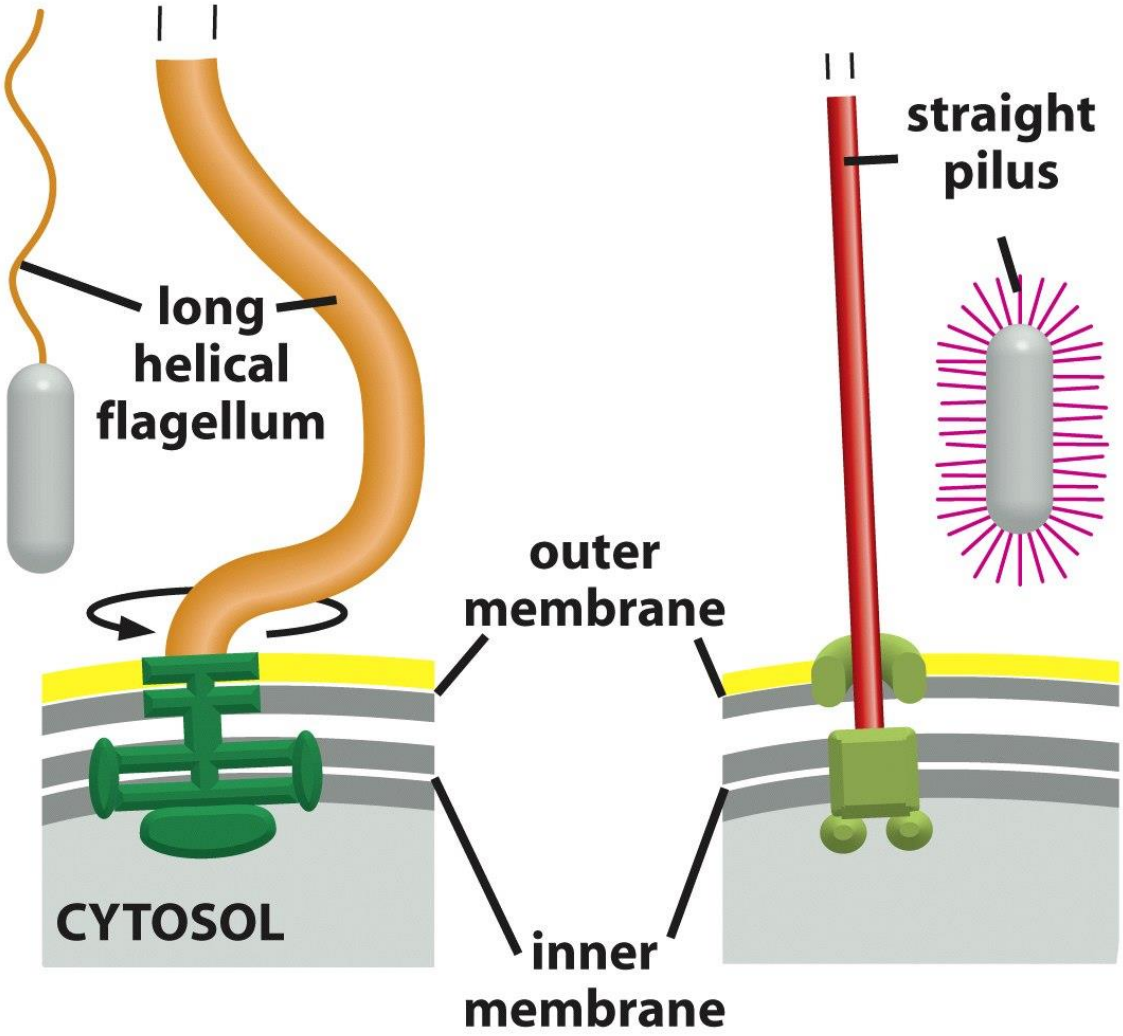
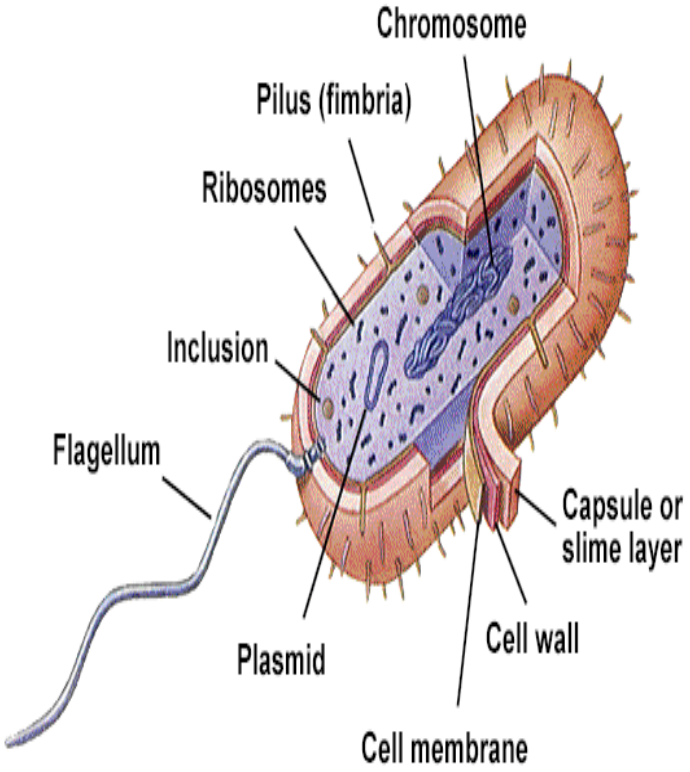


Figure 24-4d *Molecular Biology of the Cell* (© Garland Science 2008)

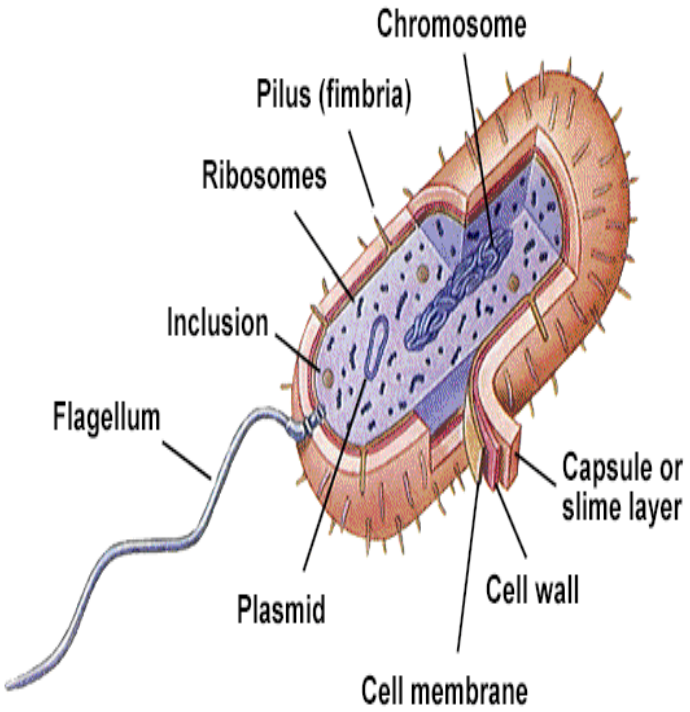
Capsule or Slime Layer

- **Glycocalyx - Polysaccharide on external surface**
- **Adhere bacteria to surface**
  - *S. mutans* and enamel of teeth
- **Prevents Phagocytosis**
  - Complement can't penetrate sugars



Cytoplasm

- **80% Water {20% Salts-Proteins)**
  - Osmotic Shock important
- **DNA is circular, Haploid**
  - Advantages of 1N DNA over 2N DNA
  - More efficient; grows quicker
  - Mutations allow adaptation to environmen quicker
- **Plasmids; extra circular DNA**
  - Antibiotic Resistance
- **No organelles (Mitochondria, Golgi, etc.)**



Cytoplasm: DNA

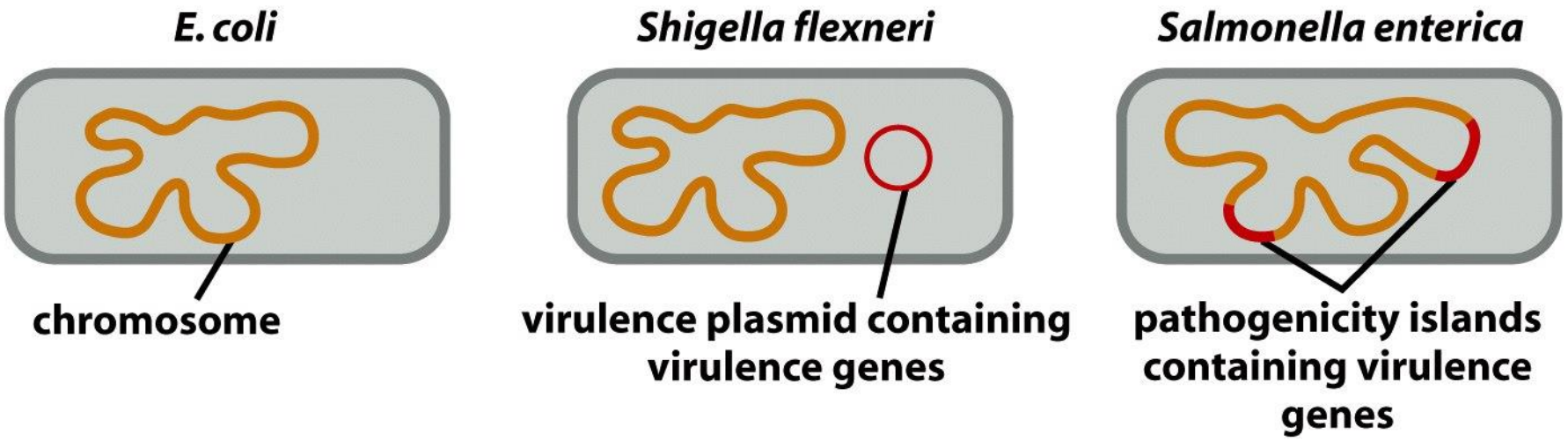
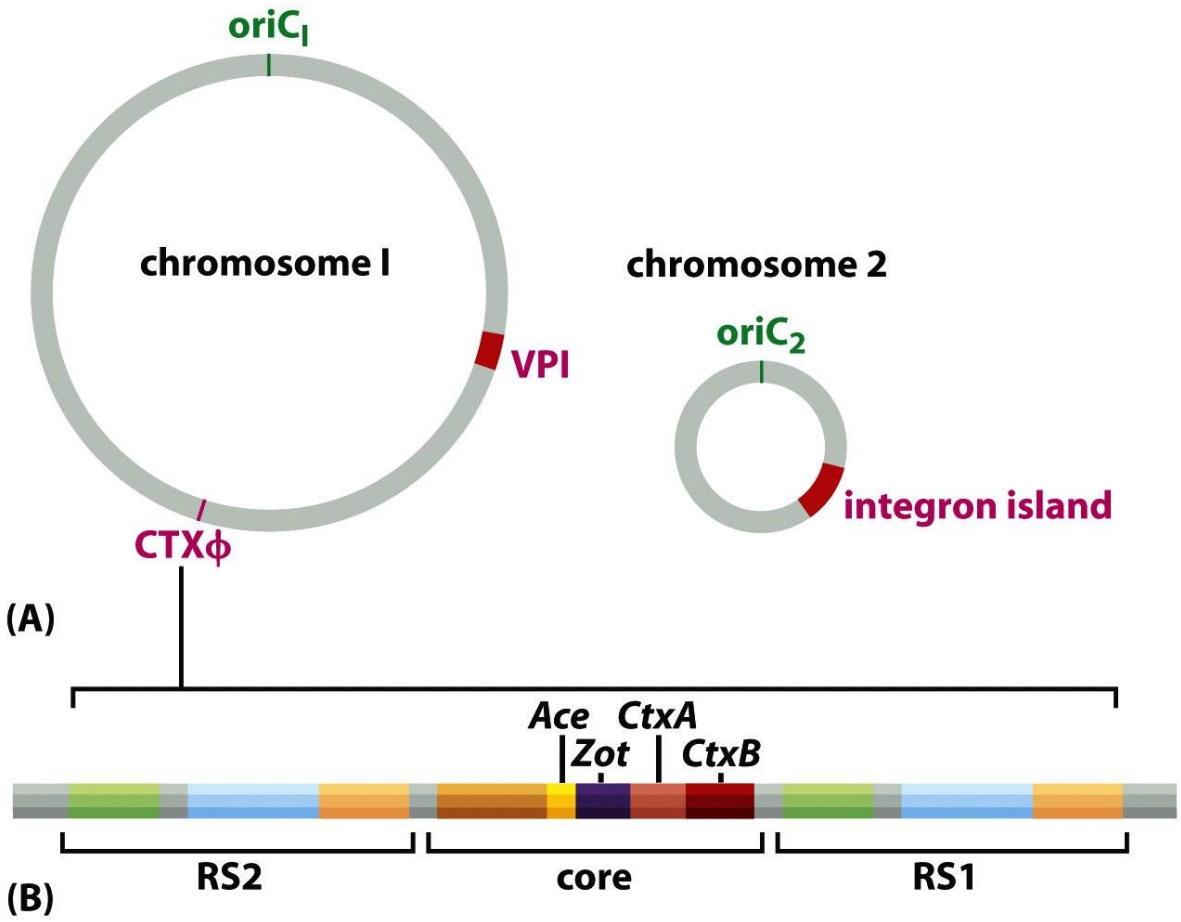


Figure 24-5 *Molecular Biology of the Cell* (© Garland Science 2008)

Vibrio cholorae

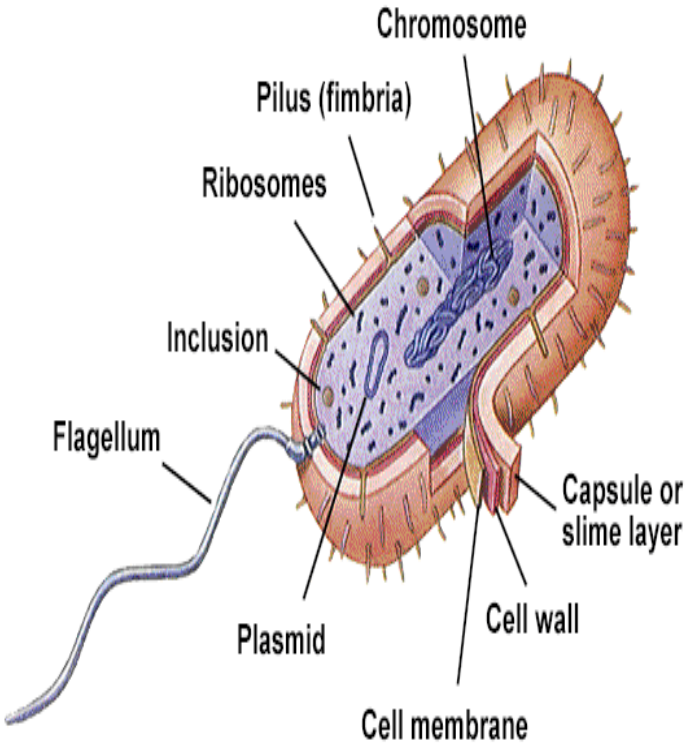


The B subunit binds to a glycolipid on epithelial cells in gut. The B subunit transfers the A into cytoplasm.
The A subunit activates adenylyl cyclase results in an overaccumulation of cyclic AMP and an ion imbalance, leading to the massive watery diarrhea associated with cholera.

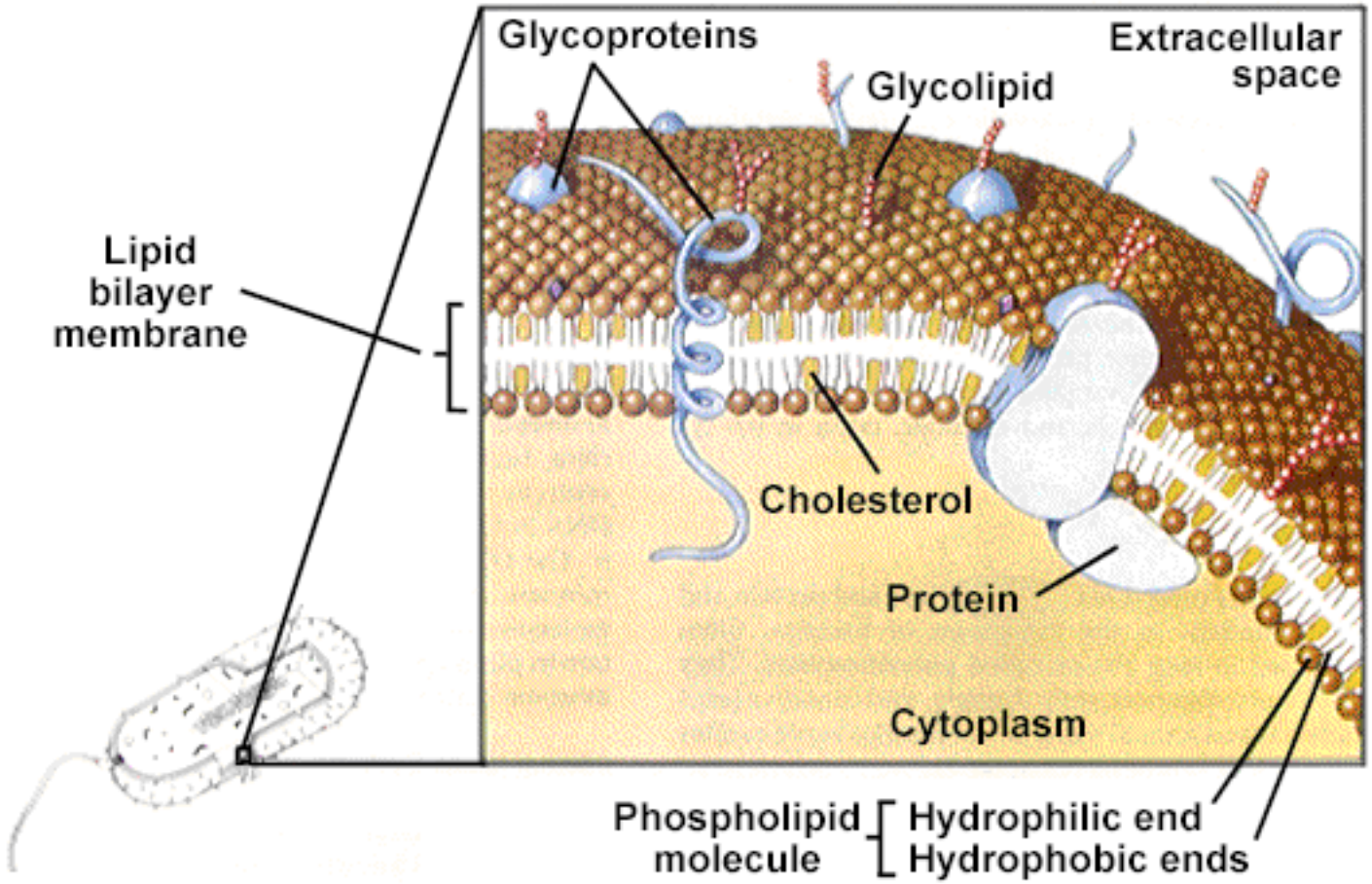
Figure 24-6a,b *Molecular Biology of the Cell* (© Garland Science 2008)

Cell Membrane

- **Bilayer Phospholipid**
- **Water can penetrate**
- **Flexible**
- **Not strong, ruptures easily**
  - Osmotic Pressure created by cytoplasm

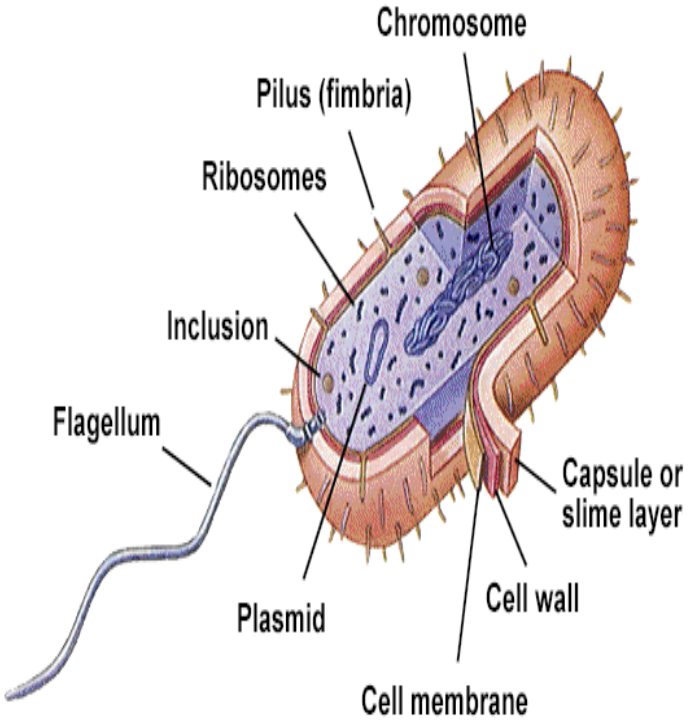


Cell Membrane

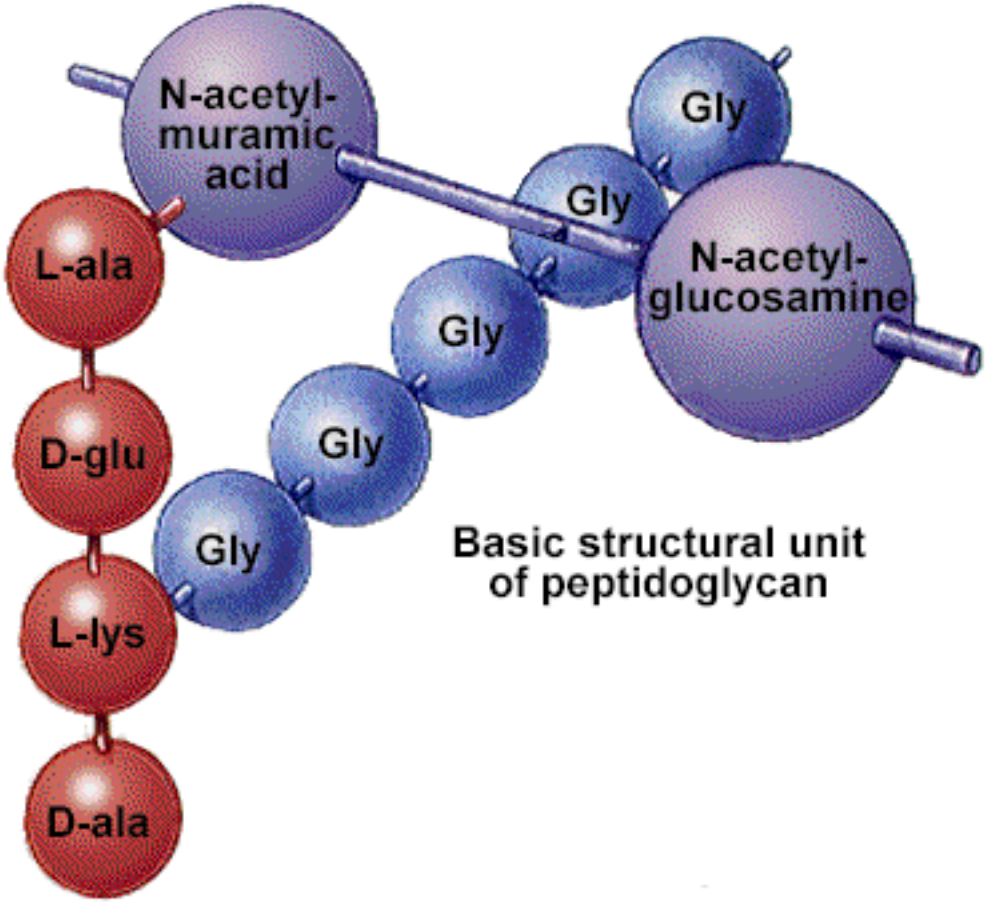


Cell Wall

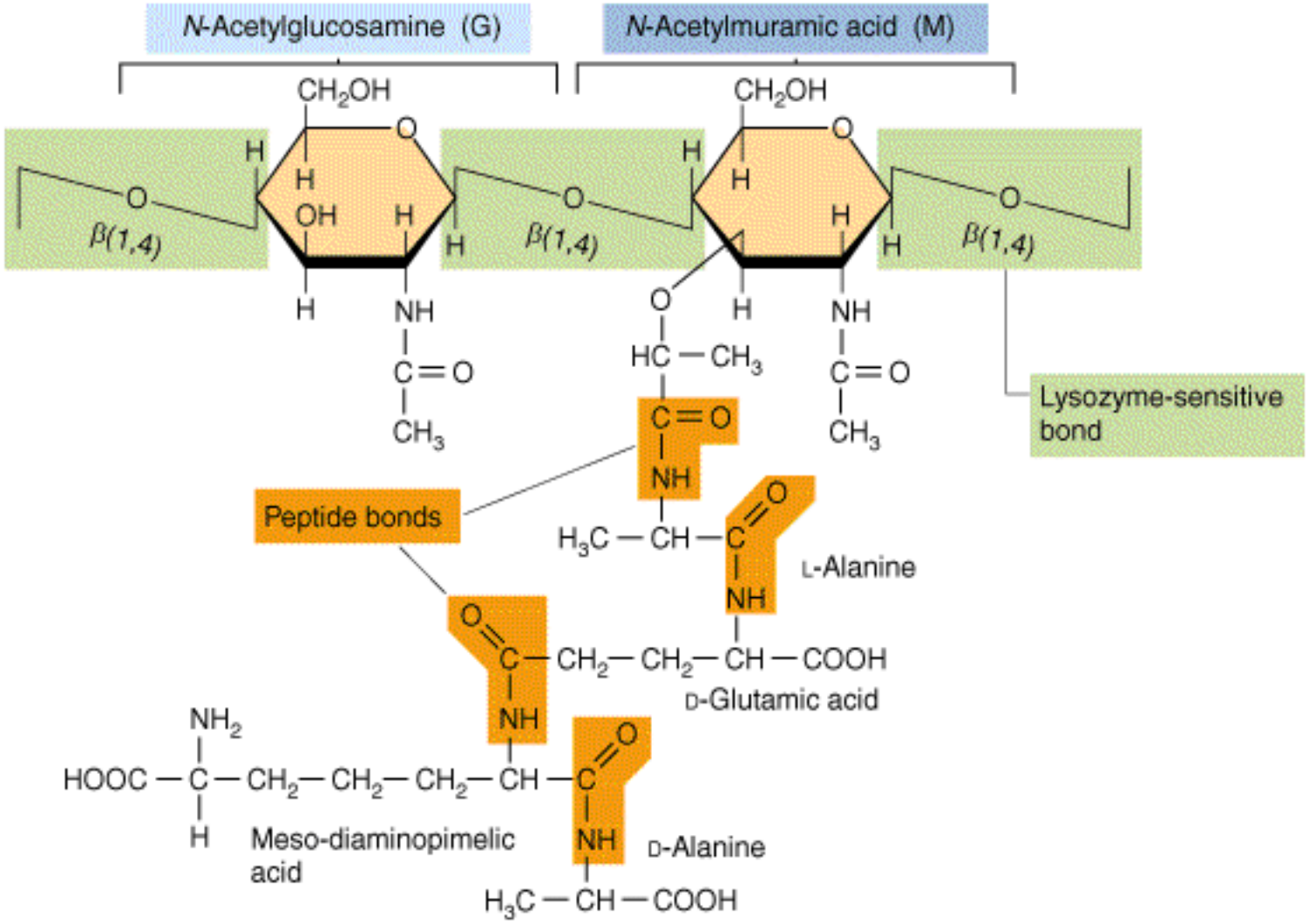
- **Peptido-glycan Polymer (amino acids + sugars)**
- **Unique to bacteria**
- **Sugars; NAG & NAM**
  - N-acetylglucosamine
  - N-acetymuramic acid
- **D form of Amino acids used not L form**
  - Hard to break down D form
- **Amino acids cross link NAG & NAM**



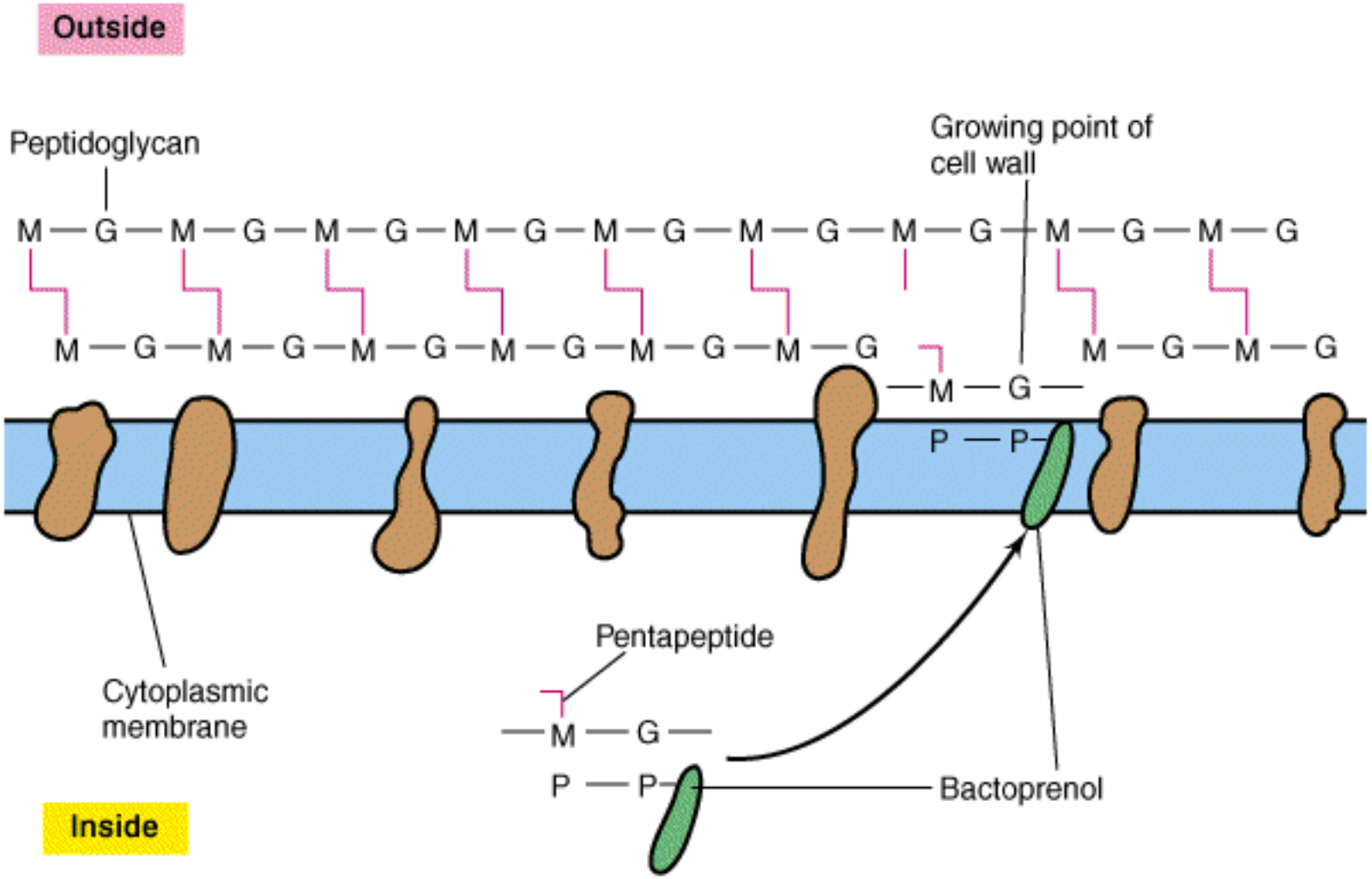
Cell Wall


N-acetyl-
muramic
acid
L-ala
D-glu
L-lys
D-ala
Gly
Gly
Gly
Gly
Gly
N-acetyl-
glucosamine
Basic structural unit
of peptidoglycan

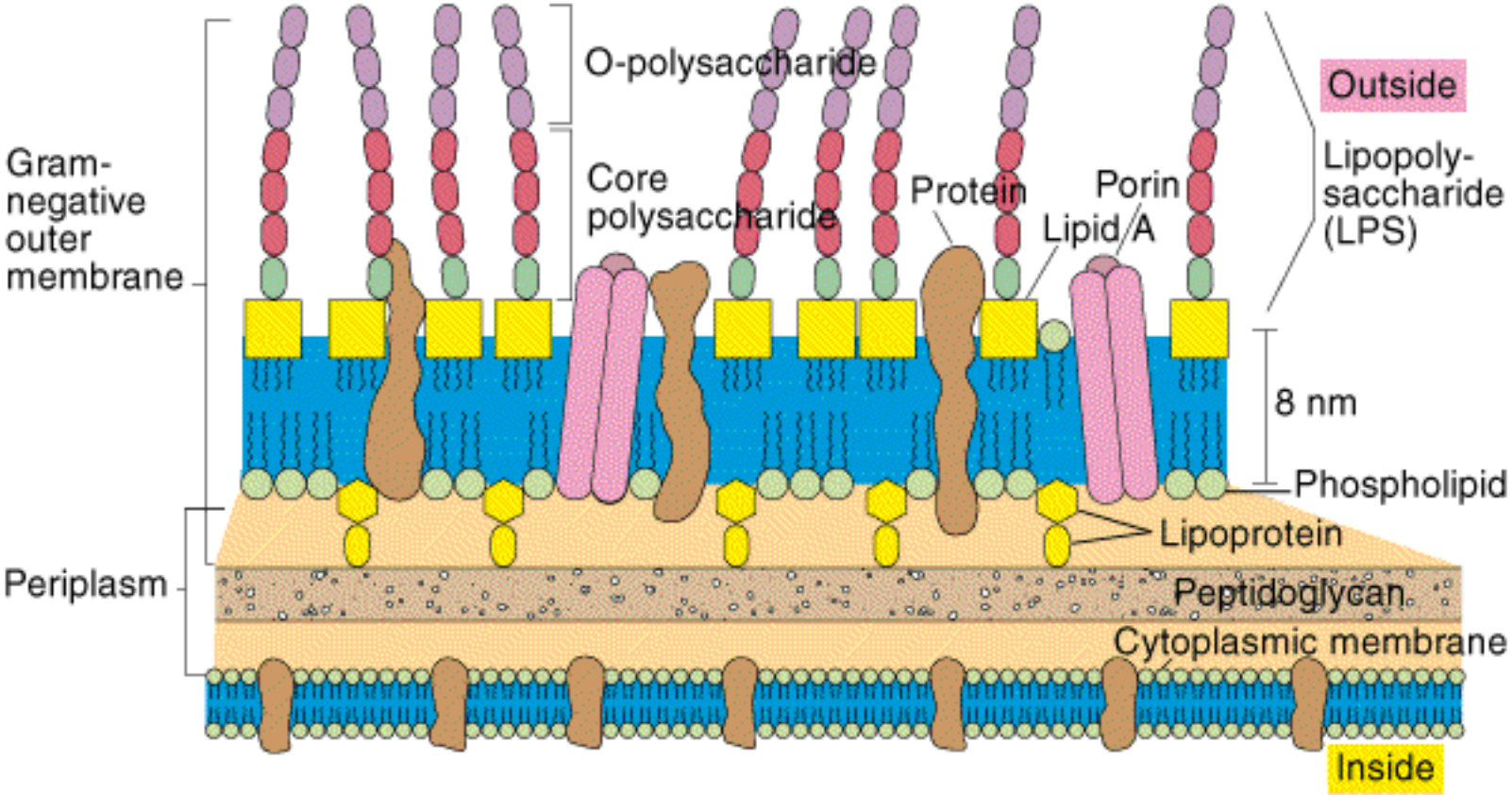
Cell Wall


N-Acetylglucosamine (G)
N-Acetylmuramic acid (M)
β(1,4)
Lysozyme-sensitive bond
Peptide bonds
L-Alanine
D-Glutamic acid
Meso-diaminopimelic acid
D-Alanine

Cell Wall


Outside
Peptidoglycan
Growing point of cell wall
M — G — M — G — M — G — M — G — M — G — M — G — M — G — M — G — M — G
M — G — M — G — M — G — M — G — M — G — M — G
M — G
P — P
Cytoplasmic membrane
Pentapeptide
M — G
P — P
Bactoprenol
Inside

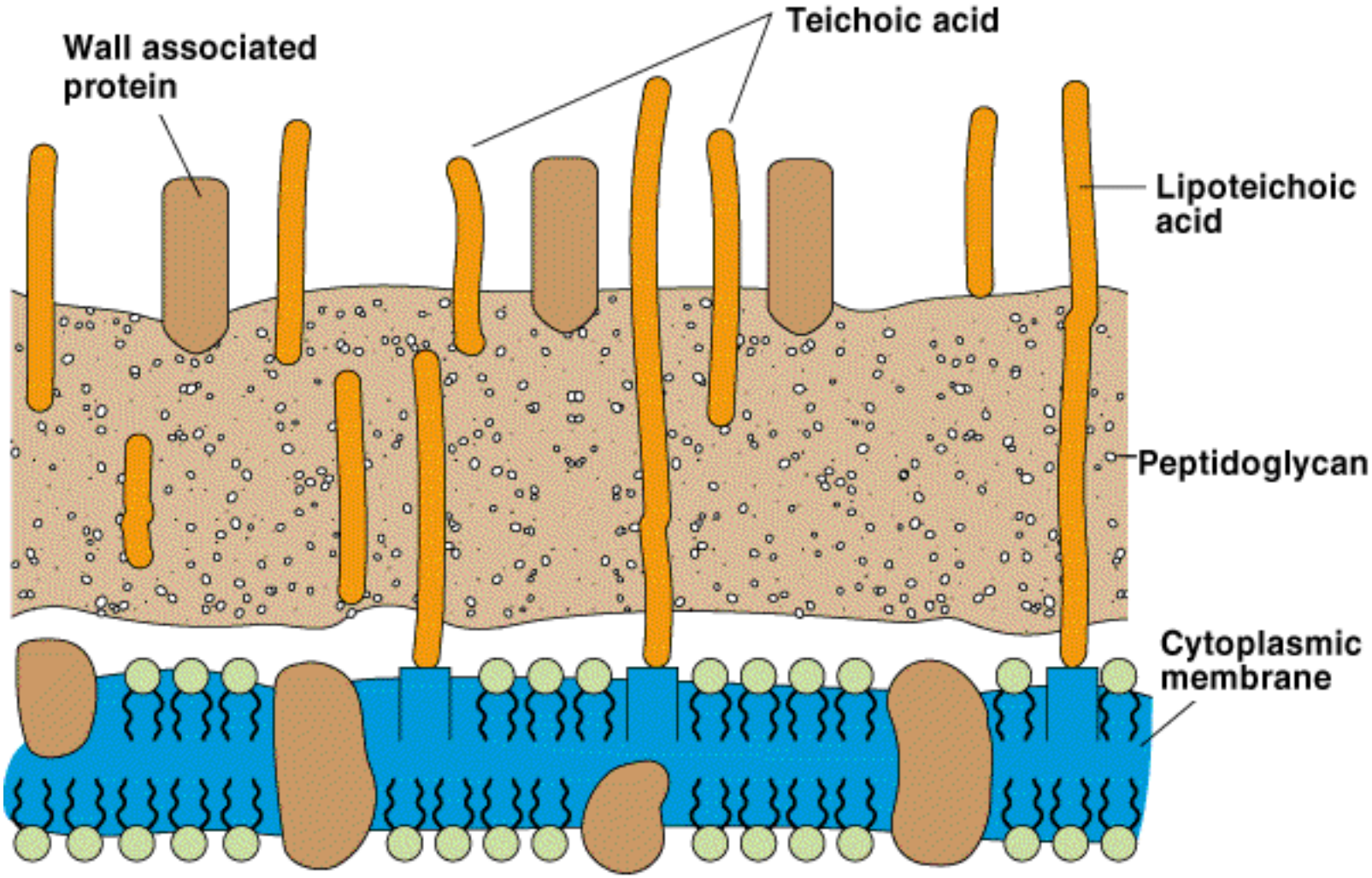
Cell Wall


Gram-
negative
outer
membrane
O-polysaccharide
Core
polysaccharide
Protein
Porin
Lipid A
Outside
Lipopoly-
saccharide
(LPS)
8 nm
Phospholipid
Lipoprotein
Periplasm
Peptidoglycan
Cytoplasmic membrane
Inside

Teichoic Acids

- Gram + only
- Glycerol, Phosphates, & Ribitol
- Attachment for Phages

Teichoic Acids

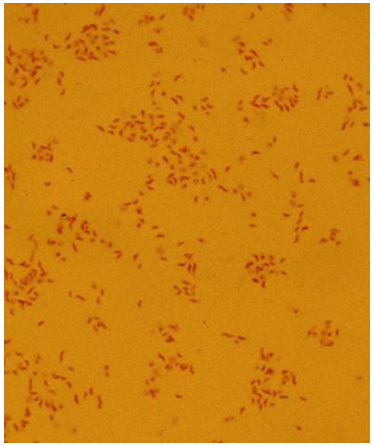


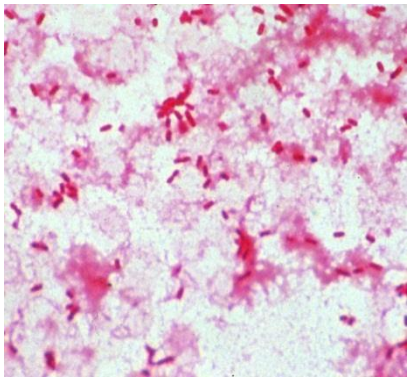
Identifying bacteria

- Size, shape, color
- Culturing techniques
- Metabolic attributes
- DNA
- The Gram's stain differentiates between two major cell wall types.
- Gram positive and Gram negative

Gram negative

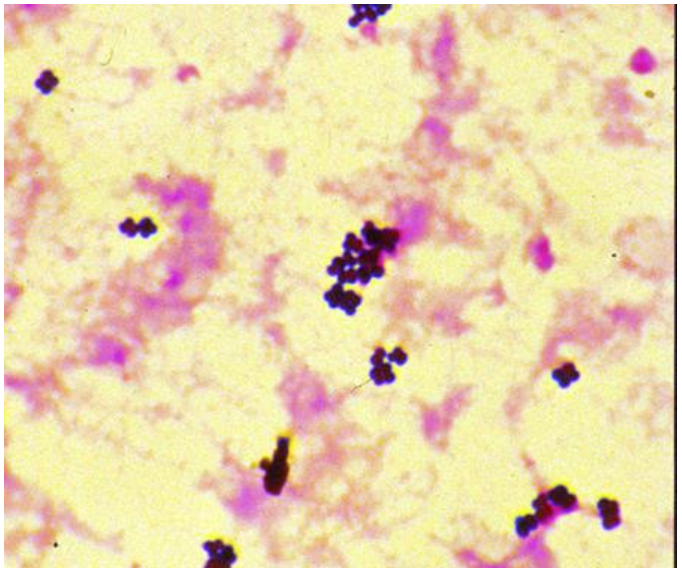
- **Gram negative species have walls containing small amounts of peptidoglycan and a lipopolysaccharide = a fat/sugar combo**
  - *Escherichia coli*, *Salmonella typhi*, *Vibrio cholerae* and *Bordetella*
  - Gram negative bacteria are harder to control with antibiotics

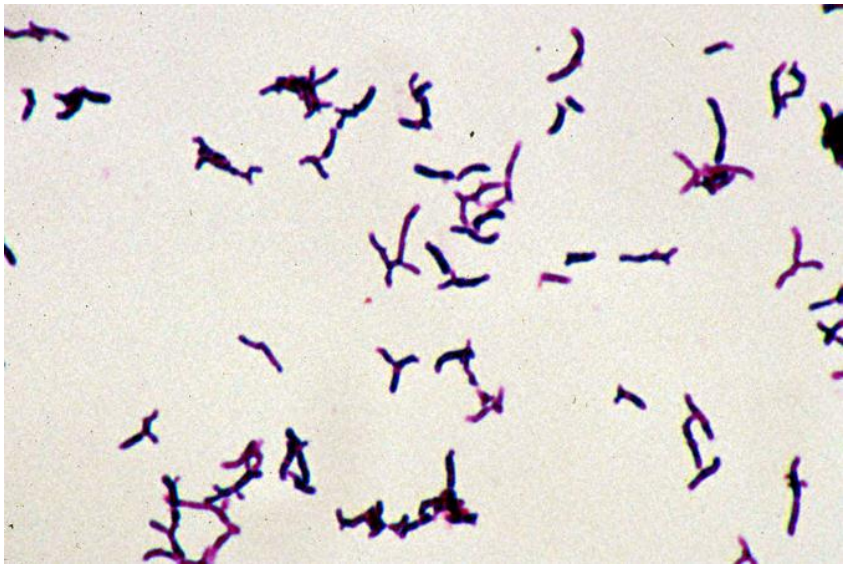




Gram positive

- **Gram positive bacteria have walls containing relatively large amounts of peptidoglycan = a starch**
  - *Staphylococcus epidermidis*, *Streptococcus pyogenes*, *Clostridium tetani, Bacillus anthacis (ANTHRAX)*





Identifying bacteria

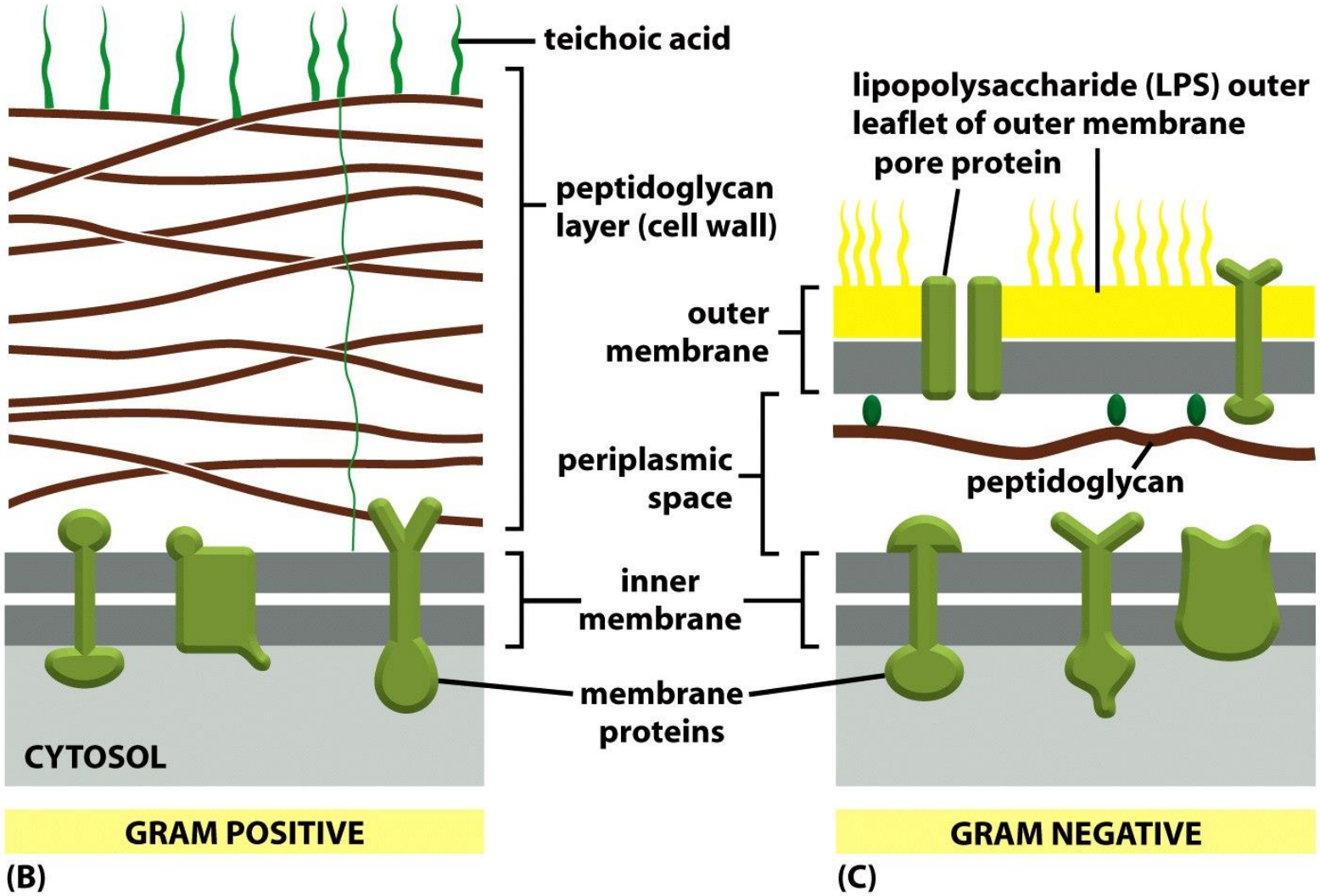
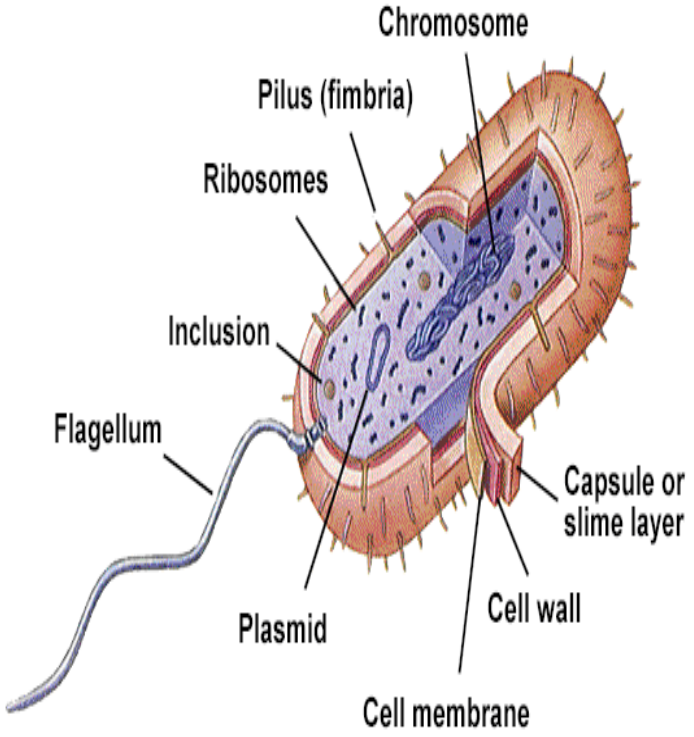


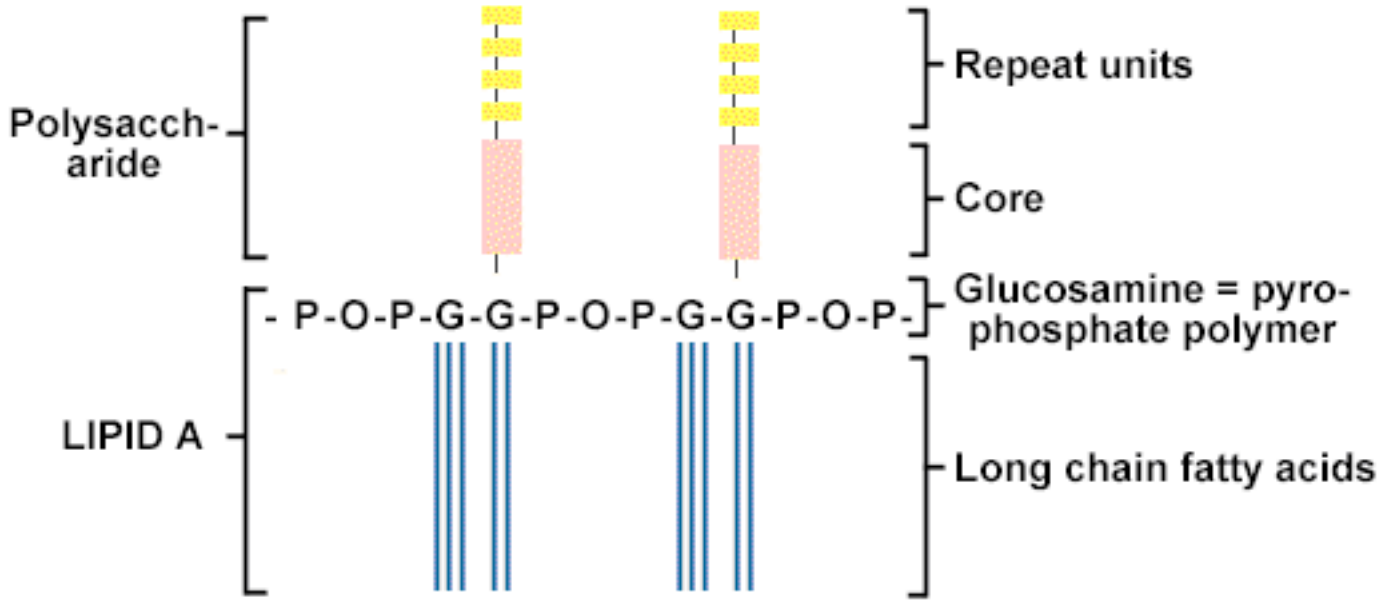
Figure 24-4b,c *Molecular Biology of the Cell* (© Garland Science 2008)

Lipopolysaccharide (LPS)

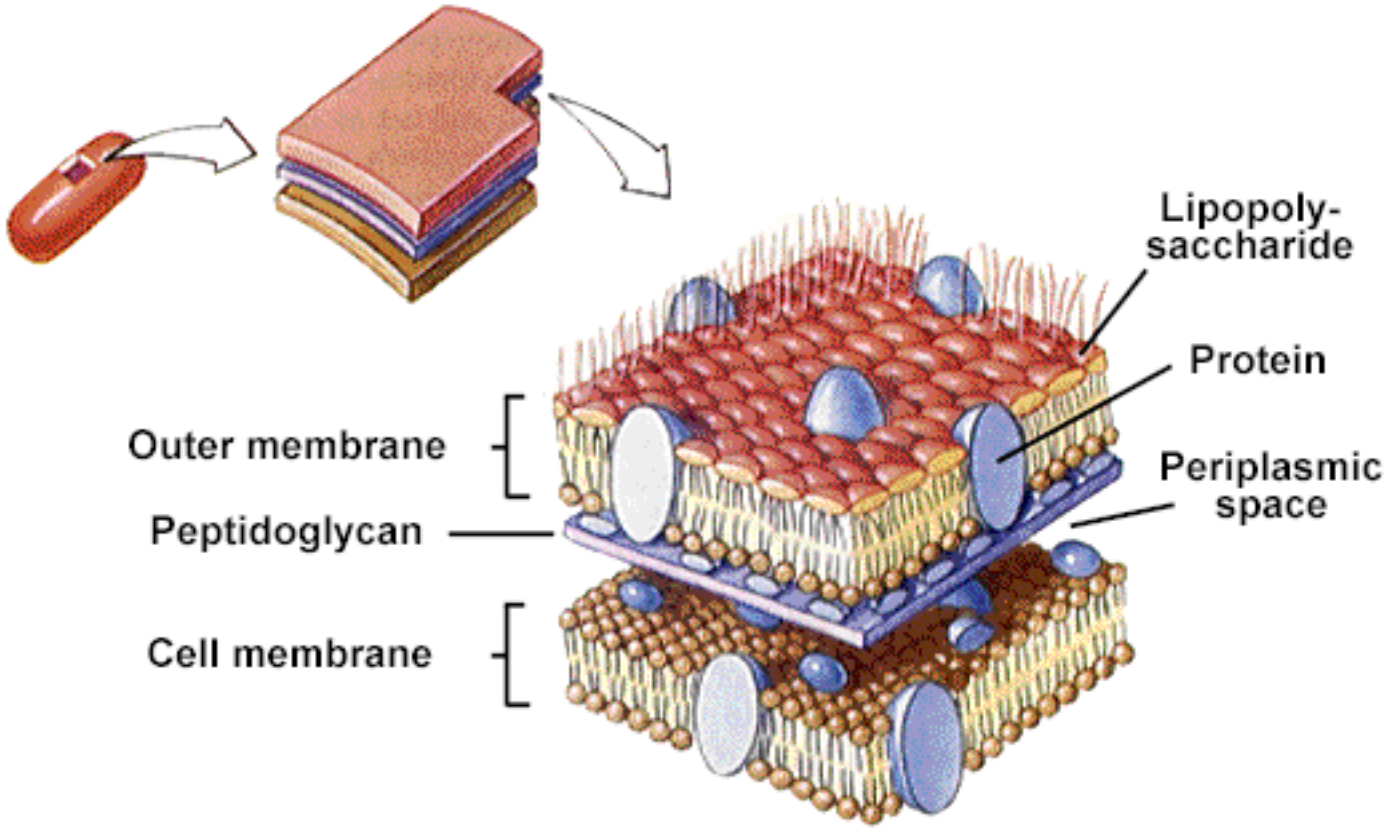
- **Endotoxin or Pyrogen**
  - Fever causing
  - Toxin nomenclature
    - Endo- part of bacteria
    - Exo- excreted into environment
- **Structure**
  - Lipid A
  - Polysaccharide
    - O Antigen of *E. coli, Salmonella*
- **G- bacteria only**
  - Alcohol/Acetone removes



Lipopolysaccharide (LPS)



Lipopolysaccharide (LPS)



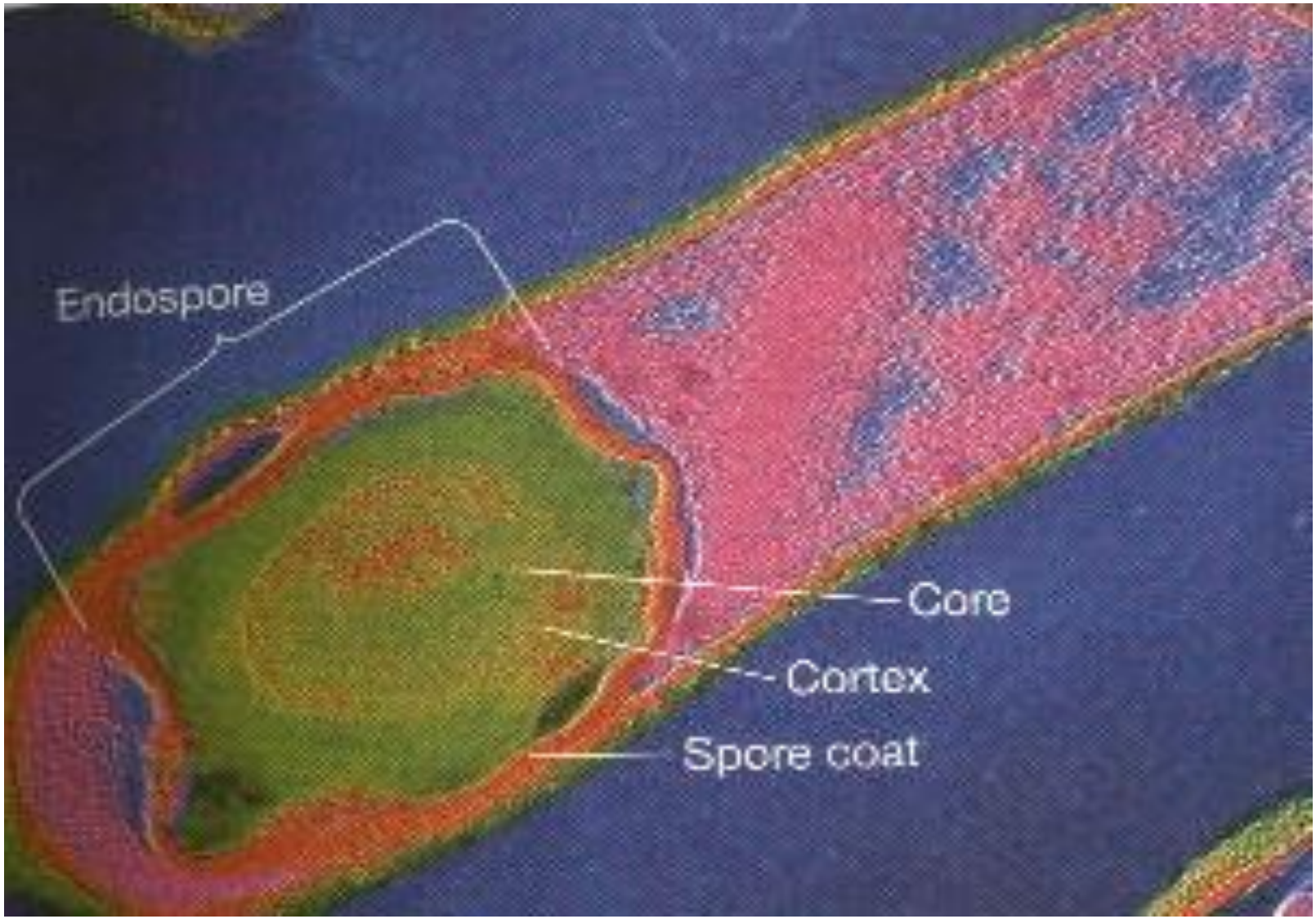
Lipopolysaccharide (LPS)

- **Functions**
  - Toxic; kills mice, pigs, humans
    - G- septicemia; death due to LPS
  - Pyrogen; causes fever
    - DPT vaccination always causes fevers
  - Adjuvant; stimulates immunity
- **Heat Resistant; hard to remove**
- **Detection (all topical & IV products)**
  - Rabbits (measure fever)
  - Horse shoe crab (Amoebocytes Lyse in presence of LPS)

Endospores

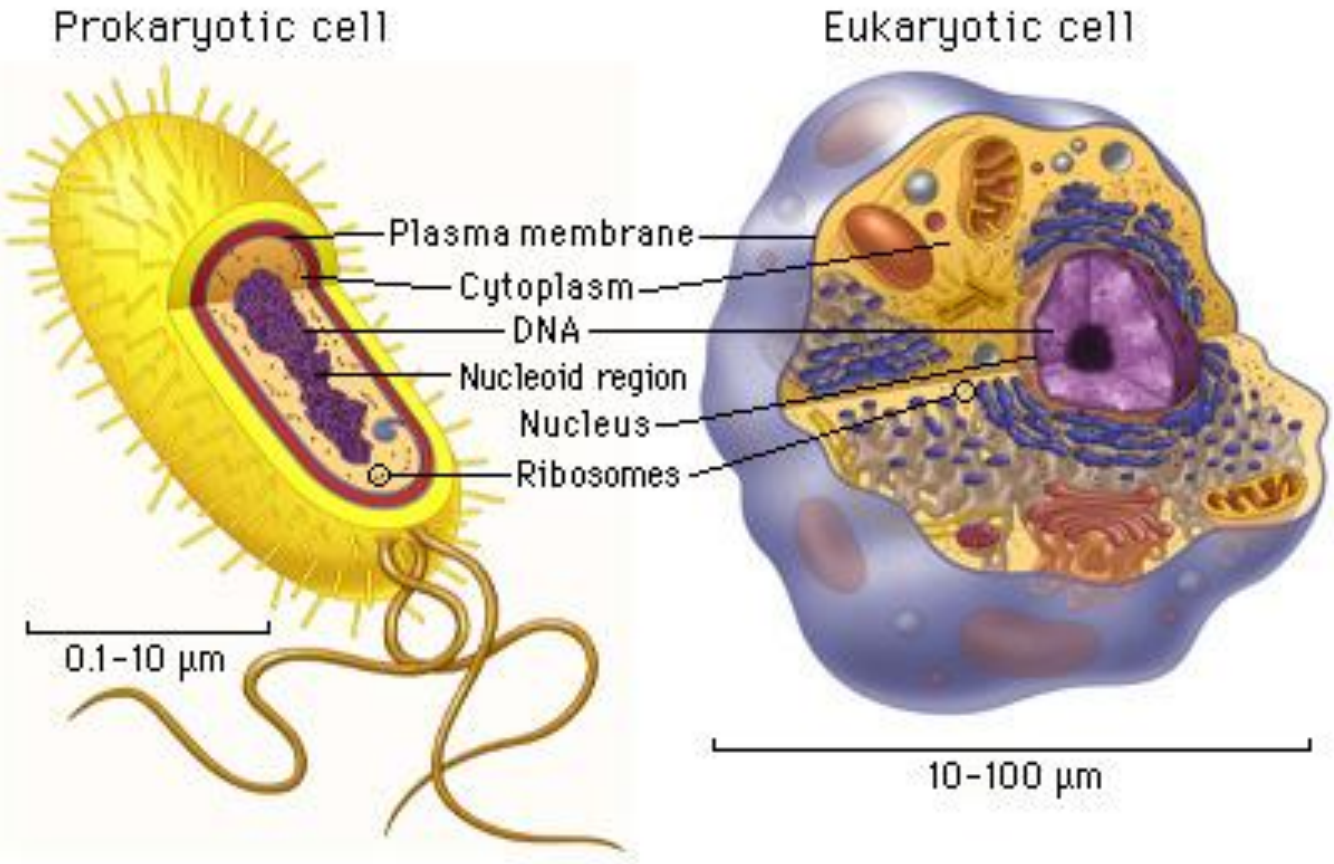
- **Resistant structure**
  - Heat, irradiation, cold
  - Boiling >1 hr still viable
- **Takes time and energy to make spores**
- **Location important in classification**
  - Central, Subterminal, Terminal
- **Bacillus stearothermophilus -spores**
  - Used for quality control of heat sterilization equipment
- **Bacillus anthracis - spores**
  - Used in biological warfare

Endospores



Prokaryotes vs. Eukaryotes

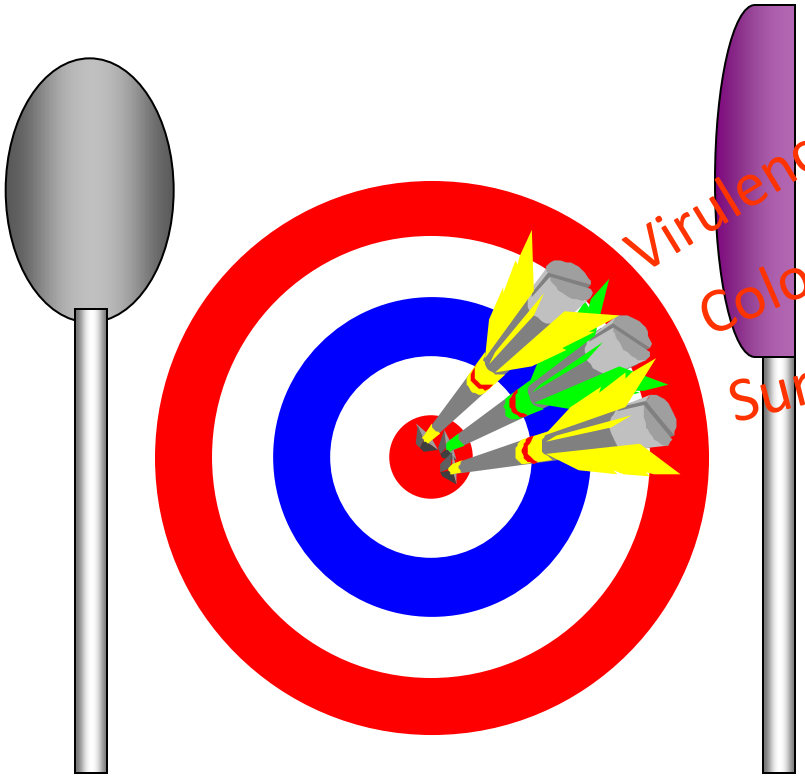
- Cell Wall
- Teichoic Acids
- LPS
- Endospores
- Circular DNA
- Plasmids



Bacterial infections

A bacterial pathogen requires virulence properties to cause disease; colonization properties for animal and/or human hosts; escape strategies to leave the host and survival properties in the environment

Example: a foodborne pathogen



Virulence properties

Colonization properties

Survival properties

A food pathogen requires virulence properties to cause disease; colonization properties for animal and human hosts; survival properties in the environment and in food

How to identify a pathogen?

Koch's postulates (1890)

search help

In 1890 the German physician and bacteriologist Robert Koch set out his celebrated criteria for judging whether a given bacteria is the cause of a given disease. Koch's criteria brought some much-needed scientific clarity to what was then a very confused field.

Bacteria are pathogens and cause an observed disease if and only if:

- The bacteria are present in every case of the disease
- The bacteria are isolated from the host with the disease and grown in pure culture
- The specific disease must be reproduced when a pure culture of the bacteria is inoculated into a healthy susceptible host
- The bacteria must be recoverable from the experimentally infected host

Animal model not always available

Not always possible

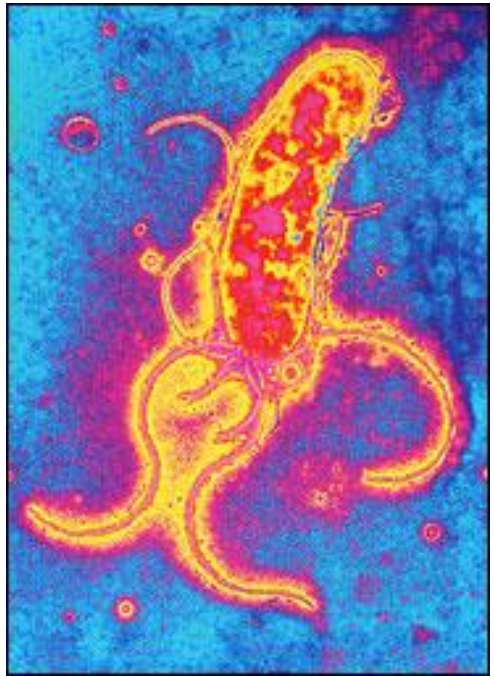
Epidemiological or immunological evidence was added

Intermezzo

Nobel Prize for Medicine 2005:
Barry Marshall and Robin Warren for the discovery of *Helicobacter pylori*

search help

From the press: "this bacterium as the cause for ulcers and 'other diseases"
A causal relationship with gastric ulcers has been proven
A causal relationship with gastric cancer is considered.
Depending on age, 10% to 80% of the population is infected (cohort effect. Add roughly 10% per decade)
Only in 10% of cases does disease occur



Have Koch's postulates been fullfilled?
Is *Helicobacter pylori* a pathogen?

There is a continuous spectrum from 'good' to 'evil'

How to identify a virulence gene?

Molecular Koch's postulates (1988)

search help

In 1988 Stanley Falkow published a commentary article translating Koch's postulates into the era of molecular biology. He described the then common approaches to identify virulence genes and listed the conclusive evidence needed:

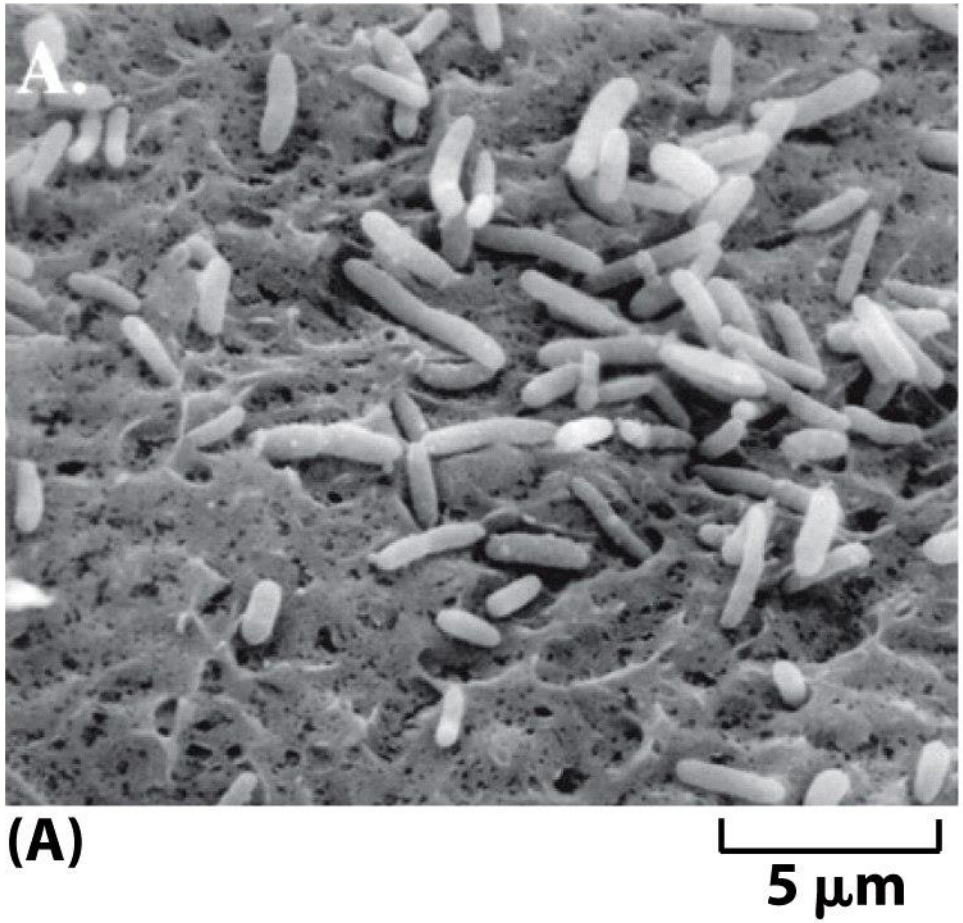
Genes are considered virulence genes if and only if:

1. The phenotype or gene is associated with pathogenic strains/species
2. Specific inactivation of the gene results in a measurable loss in virulence (attenuation)
3. Reversion or allelic replacement of the mutated gene restores pathogenicity
4. Or to 2,3: induction of specific antibodies neutralizes pathogenicity

Bacterial pathogens

- **Bacteria that make you sick**
  - Why do they make you sick?
    - To get food they need to survive and reproduce
  - How do they make you sick?
    - They produce poisons (toxins) that result in fever, headache, vomiting, and diarrhea and destroy body tissue

Bacterial pathogens



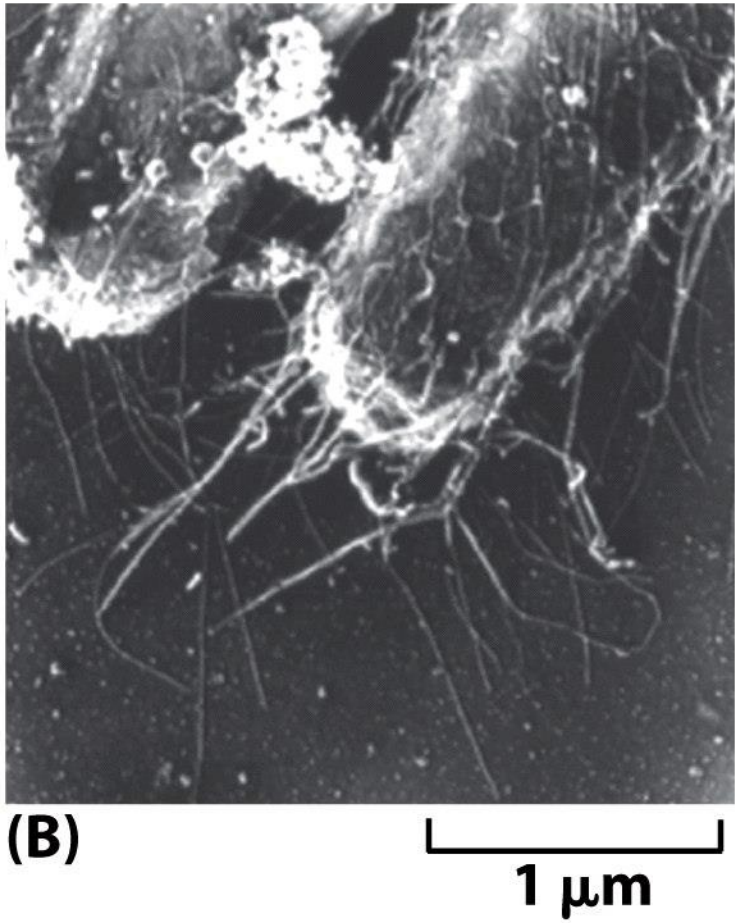
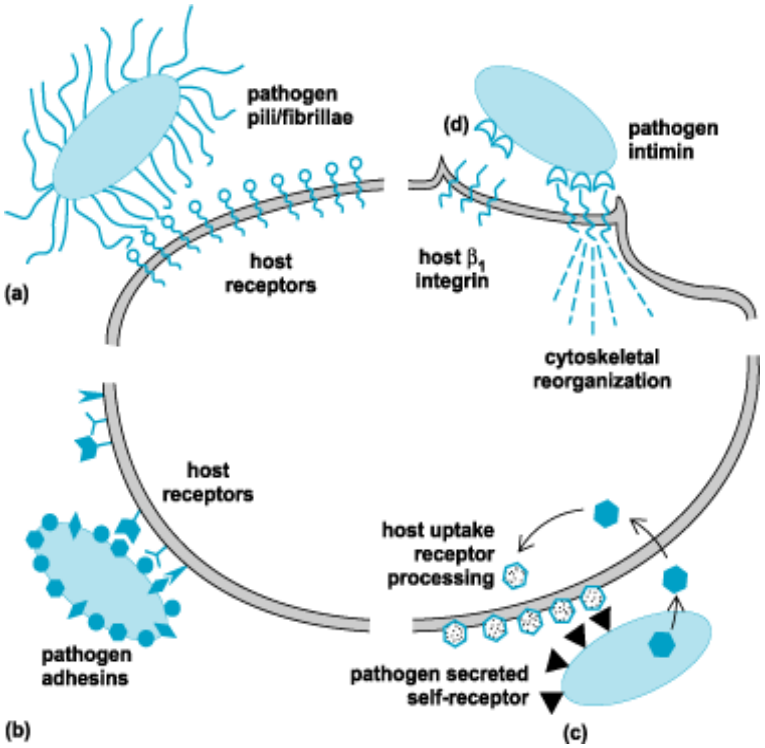


Figure 24-21 *Molecular Biology of the Cell* (© Garland Science 2008)

Cell surface receptors



Adhesion is central to host:pathogen interaction

Interactions can be via

a) host receptors binding to pili/fimbriae

b) adhesion proteins binding to host receptors

c) pathogen secreted receptors

d) host integrin binding to receptors

http://www.cdc.gov/ncidod/eid/vol5no3/wizeman.htm)

Bacteria are phagocytosed

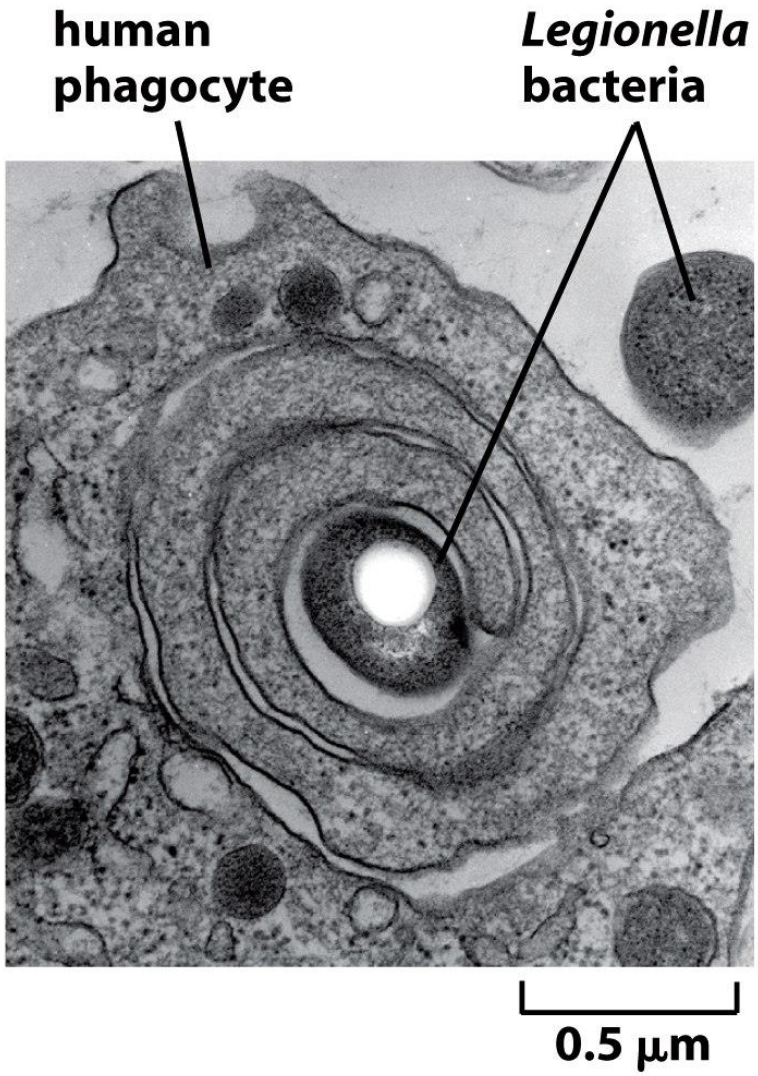


Figure 24-25 *Molecular Biology of the Cell* (© Garland Science 2008)

Bacteria induce phagocytosis

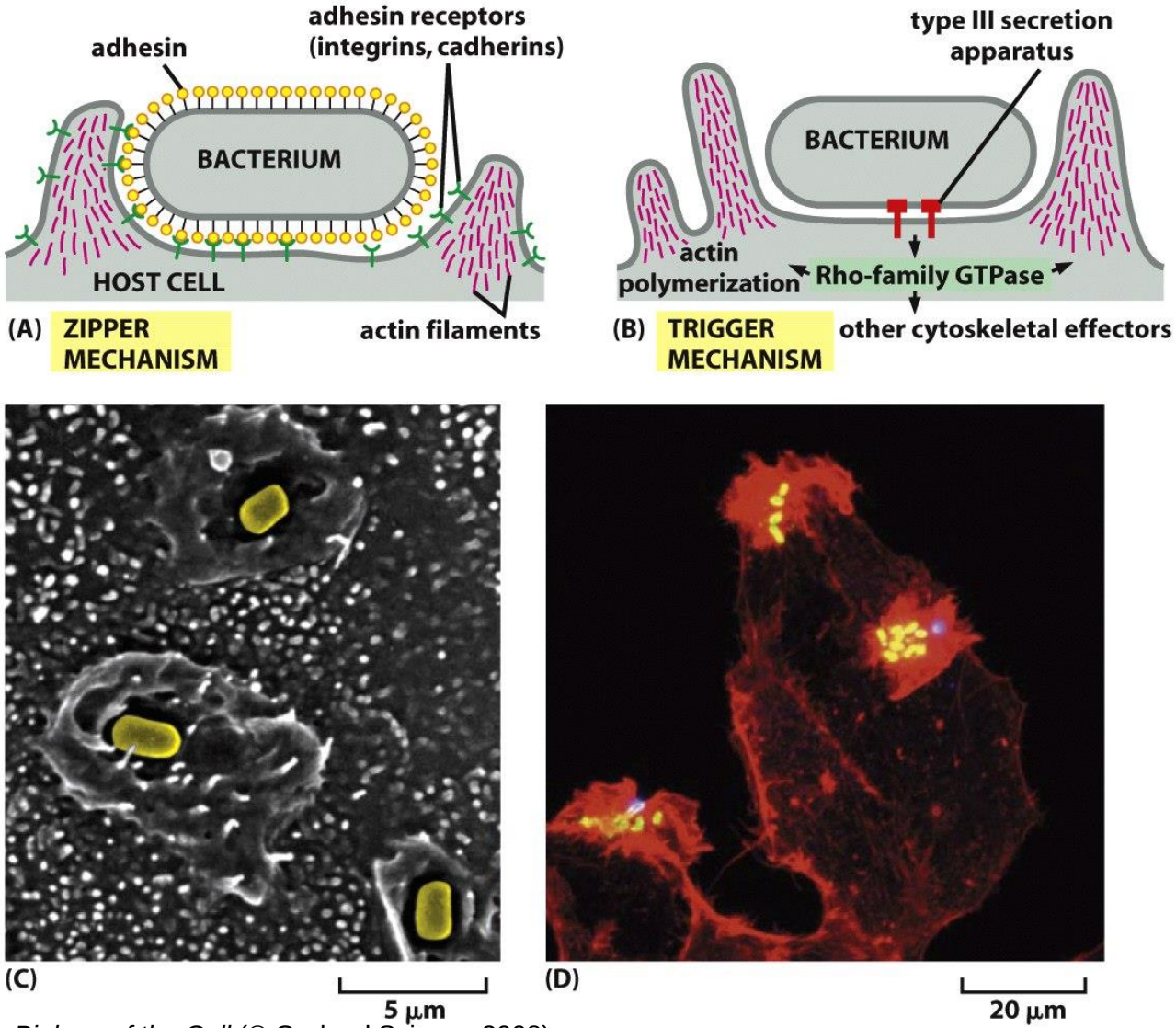
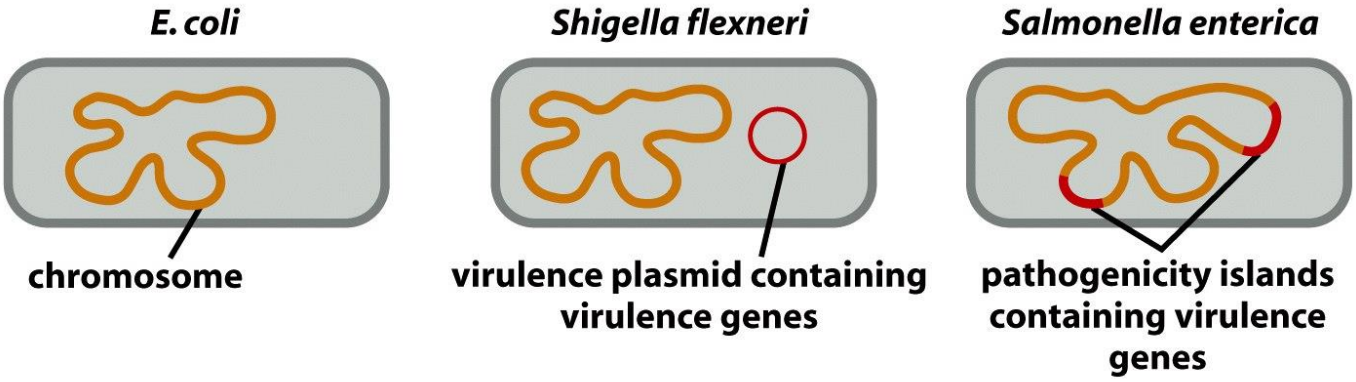


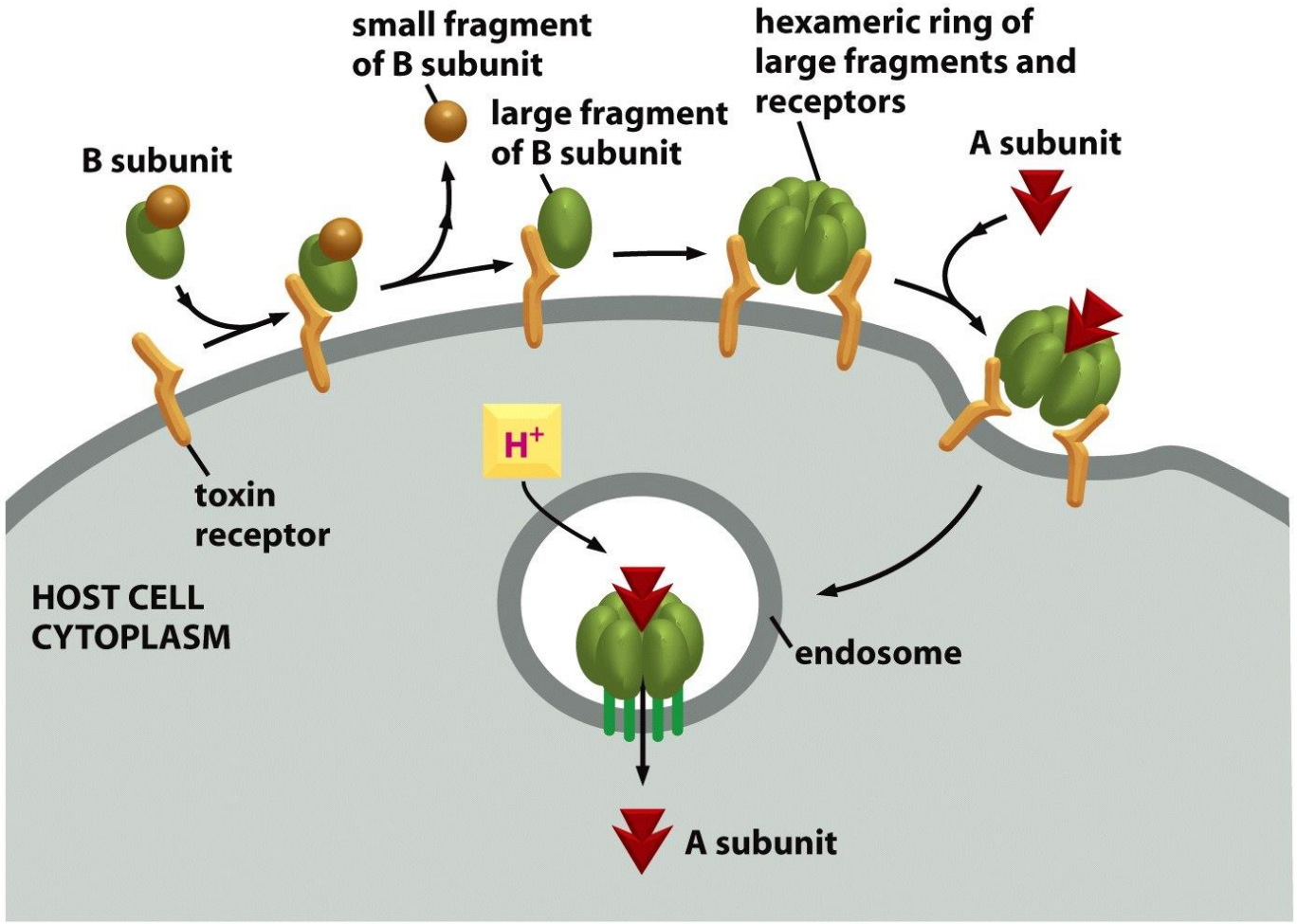
Figure 24-26 *Molecular Biology of the Cell* (© Garland Science 2008)

Pathogenicity islands and virulence factors

- **Genes within PAI are upregulated during infection to promote colonization and disease**
  - This is achieved with dedicated transcription regulators
    - Mga (multigene activator)
    - Two component regulatory systems
      - Transcriptome variation during progression of disease
        - Entrance, survival, colonization, invasiveness
  - Toxins (a variety of produced)
  - Surface proteins for adhesion, target destruction
    - ScpA (C5a peptidase), Sic (streptococcal inhibitor of complement)
    - ScpC (cleaves IL-8) during invasive disease
      - Avoid the host immune response by reducing neutrophil recruitment to sites of infection



Bacterial toxins: *Bacillus anthracis*



The B toxin is adenylyl cyclase producing cAMP and an ion imbalance. A toxin is a protease that cleaves MAPK

Figure 24-7a *Molecular Biology of the Cell* (© Garland Science 2008)

Intracellular pathogens: pathways

(1):
- all viruses
- *Trypansoma cruzi,*
- *Listeria monocytogenes*
- *Shigella flexneri.*

(2) :
- *Mycobacterium tuberculosis*
- *Salmonella enterica*
- *Legionella pneumophila*
- *Chlamydia trachomatis.*

(3)
- *Coxiella burnetii*
- *Leishmania.*

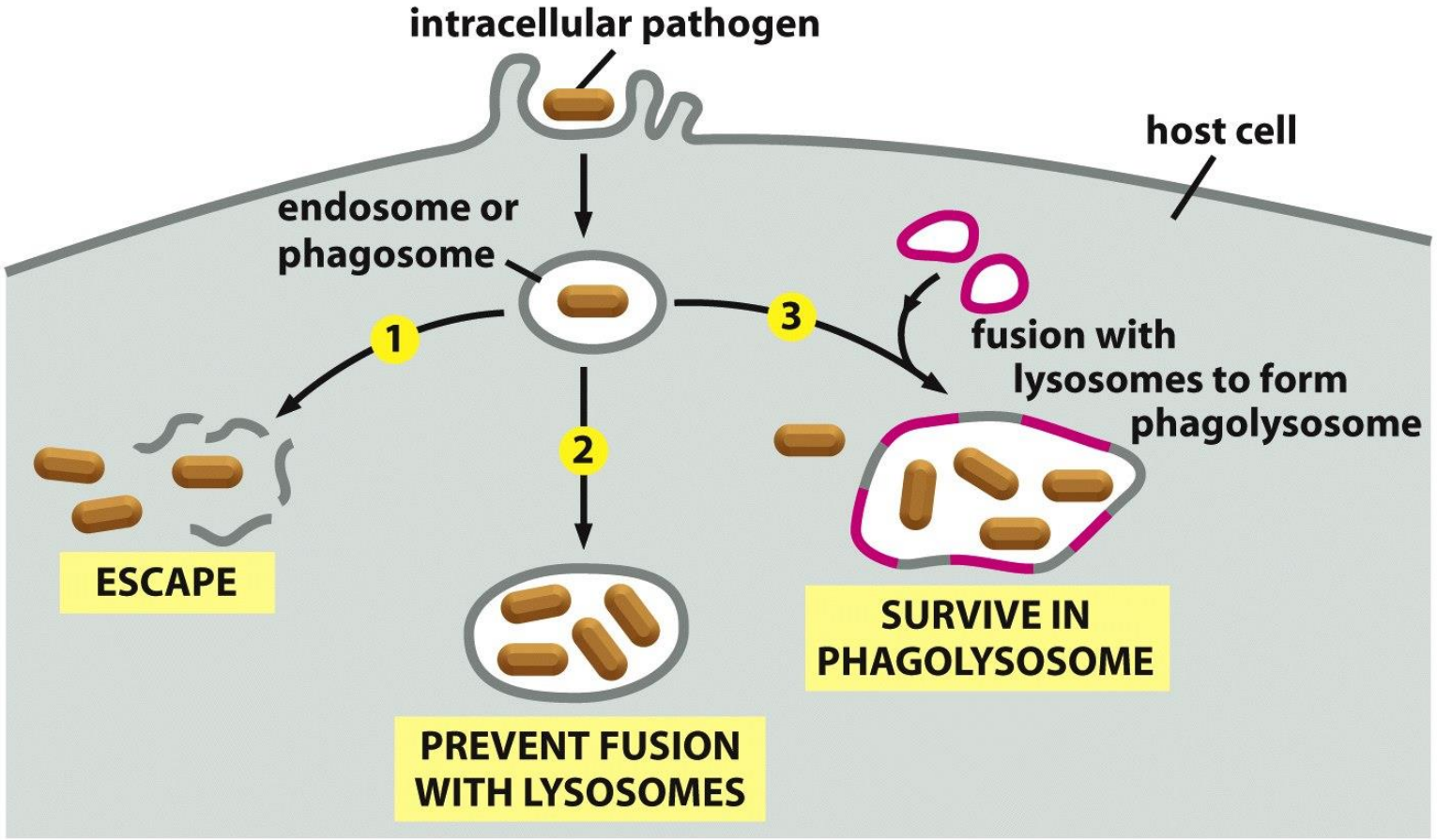


Figure 24-30 *Molecular Biology of the Cell* (© Garland Science 2008)

phagolysosome destruction

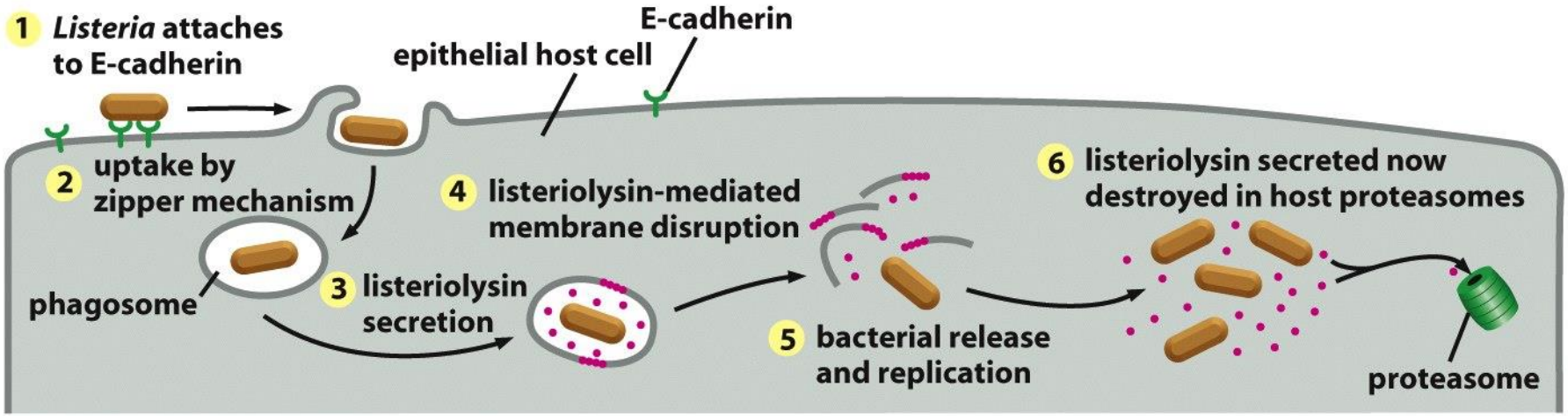


Figure 24-31 *Molecular Biology of the Cell* (© Garland Science 2008)

Modification of host trafficking

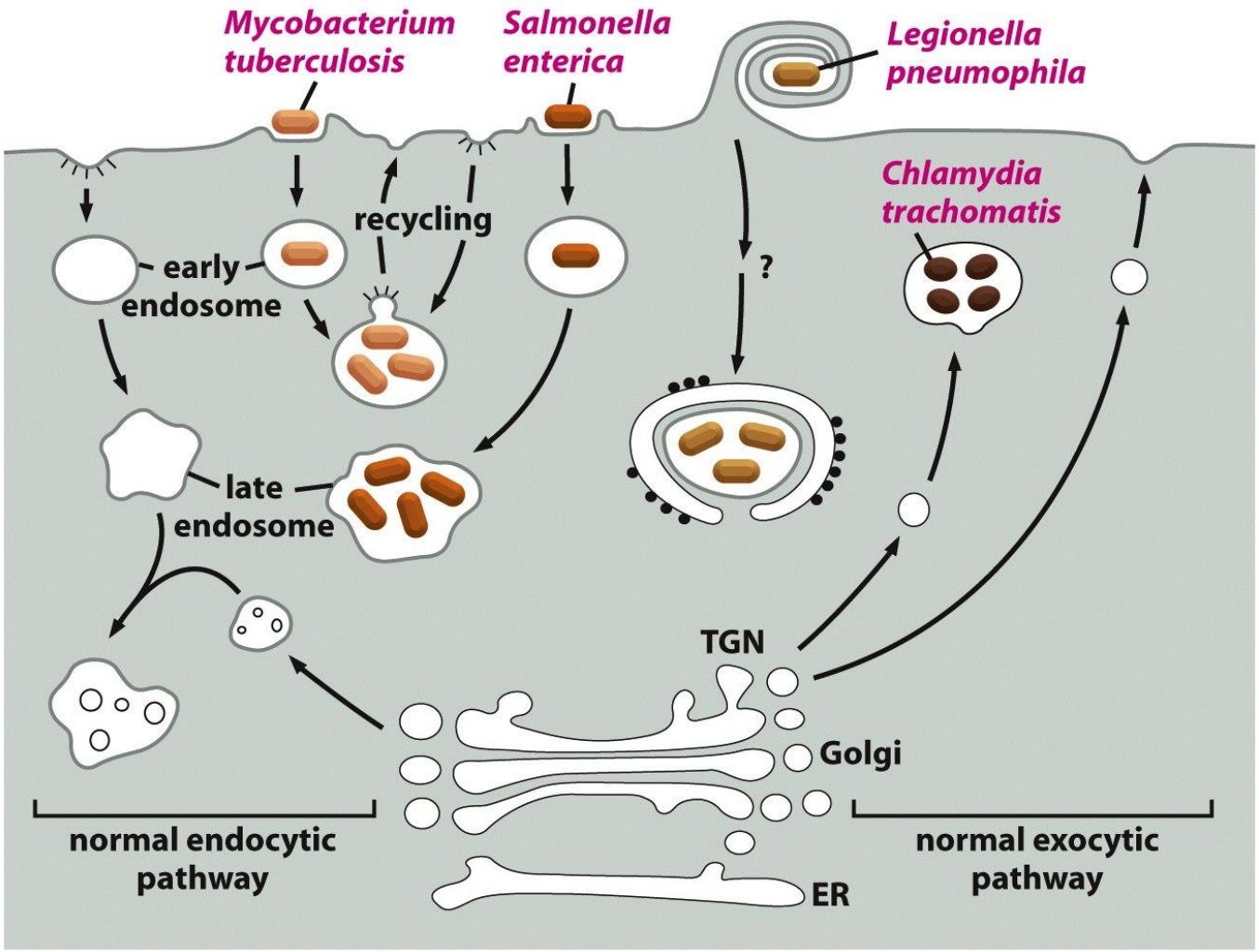
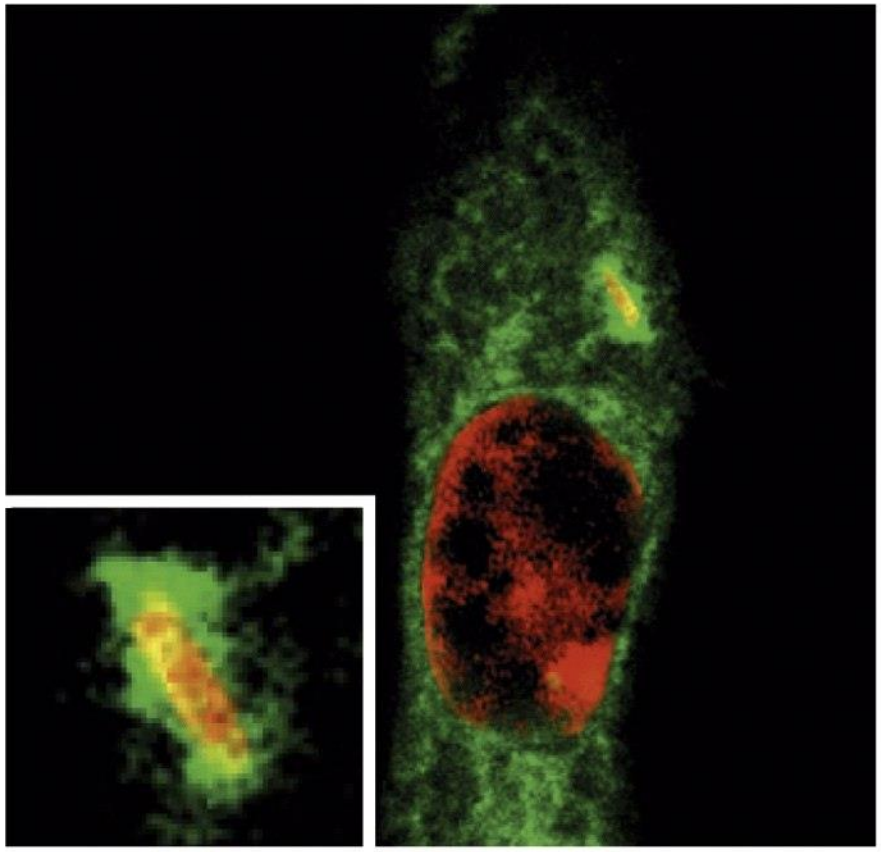


Figure 24-32 *Molecular Biology of the Cell* (© Garland Science 2008)

Intracellular pathogens



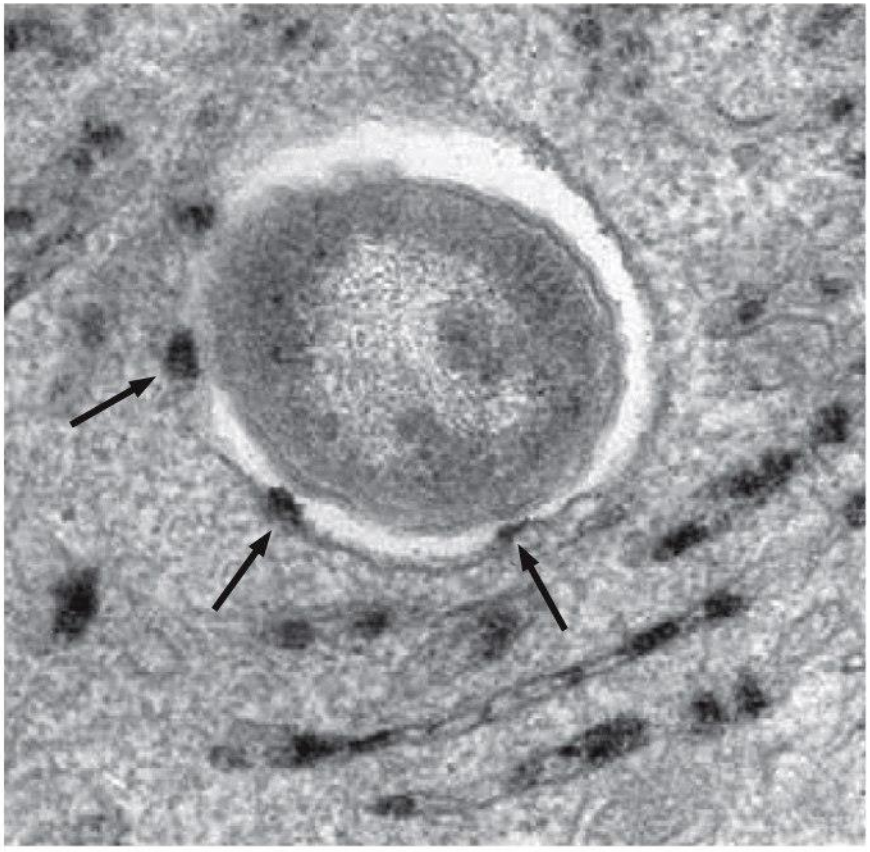


Figure 24-33 *Molecular Biology of the Cell* (© Garland Science 2008)

Intracellular pathogens

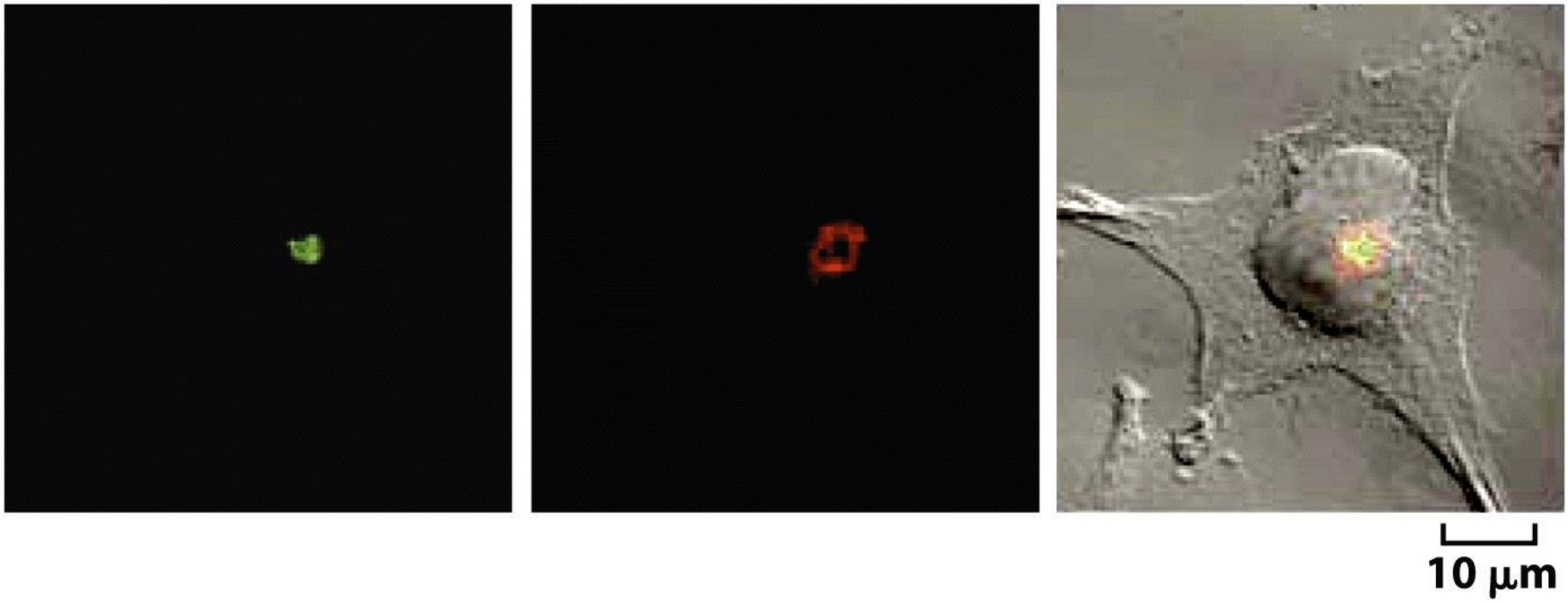


Figure 24-34a *Molecular Biology of the Cell* (© Garland Science 2008)

Intracellular pathogens

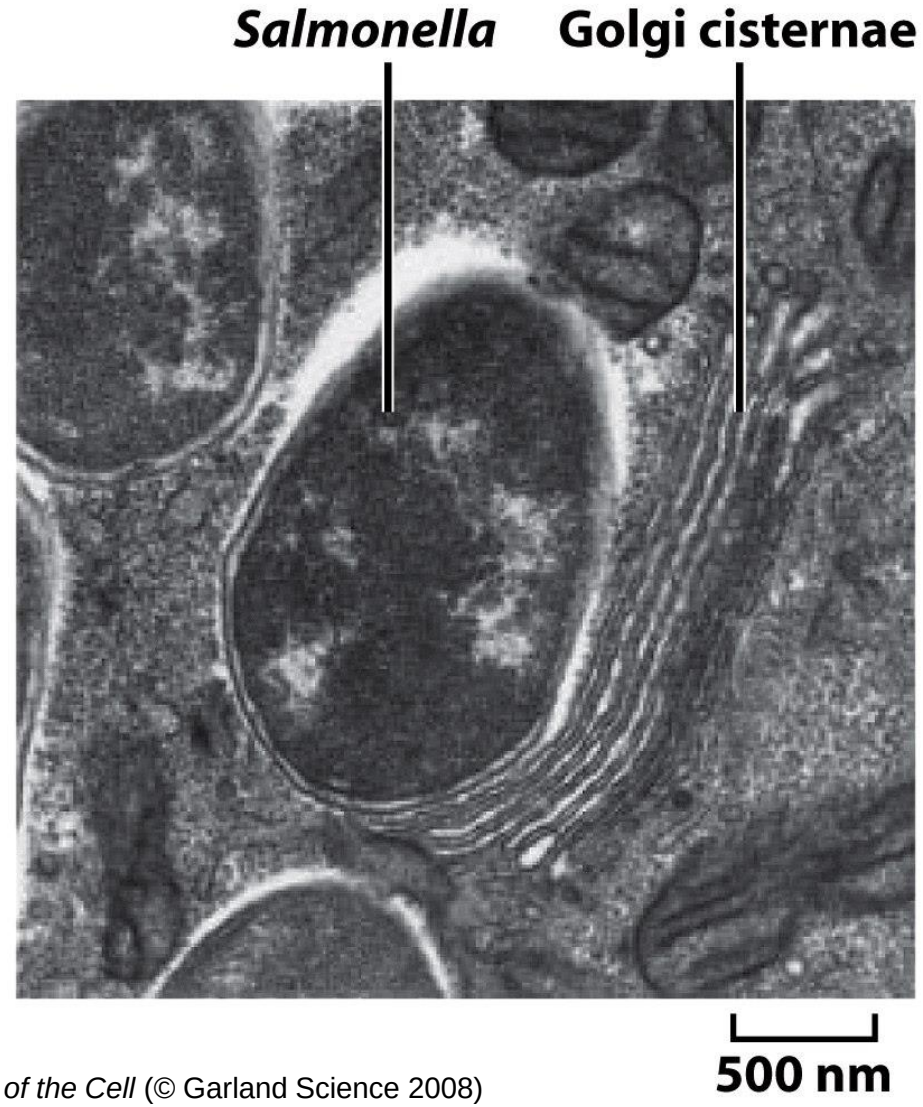


Figure 24-34b *Molecular Biology of the Cell* (© Garland Science 2008)

Bacteria hijack host actin

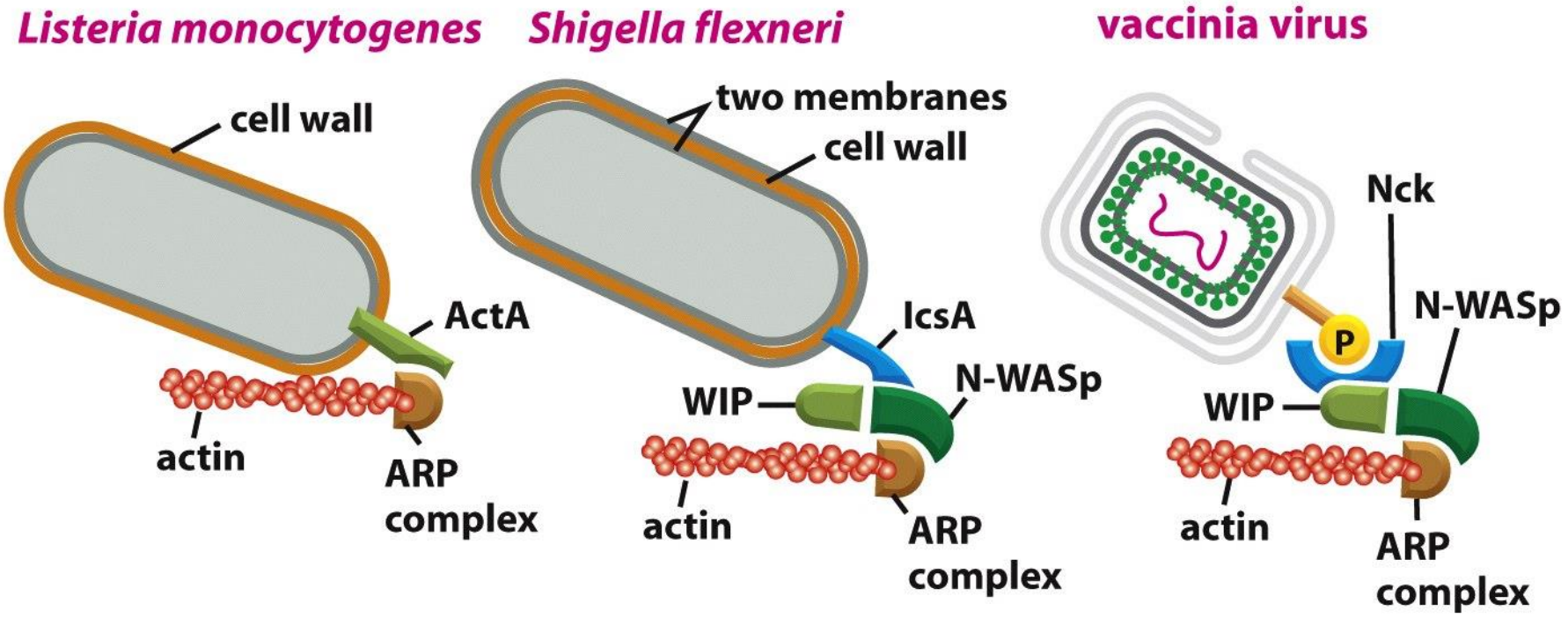


Figure 24-38 *Molecular Biology of the Cell* (© Garland Science 2008)

Wolbachia hijack host microtubules

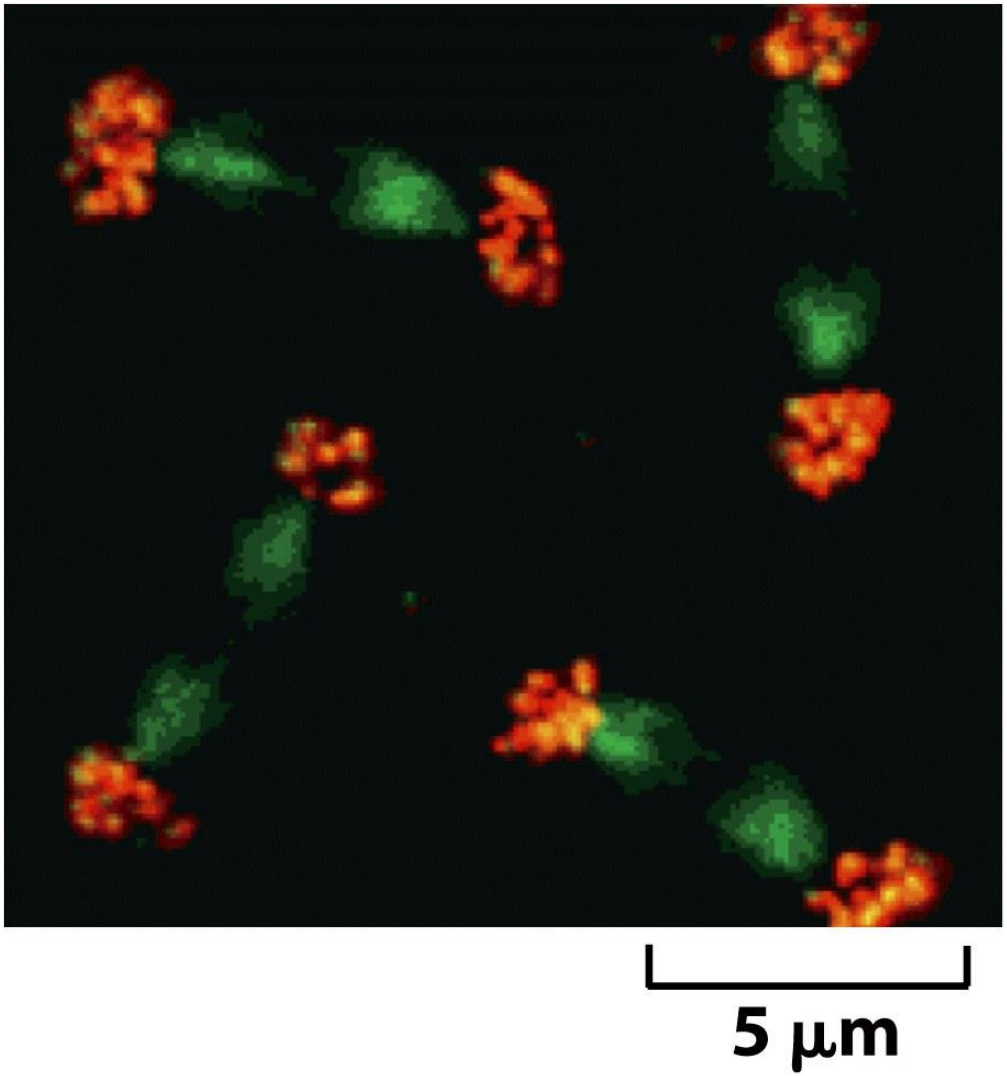


Figure 24-40 *Molecular Biology of the Cell* (© Garland Science 2008)

Antibiotic targets

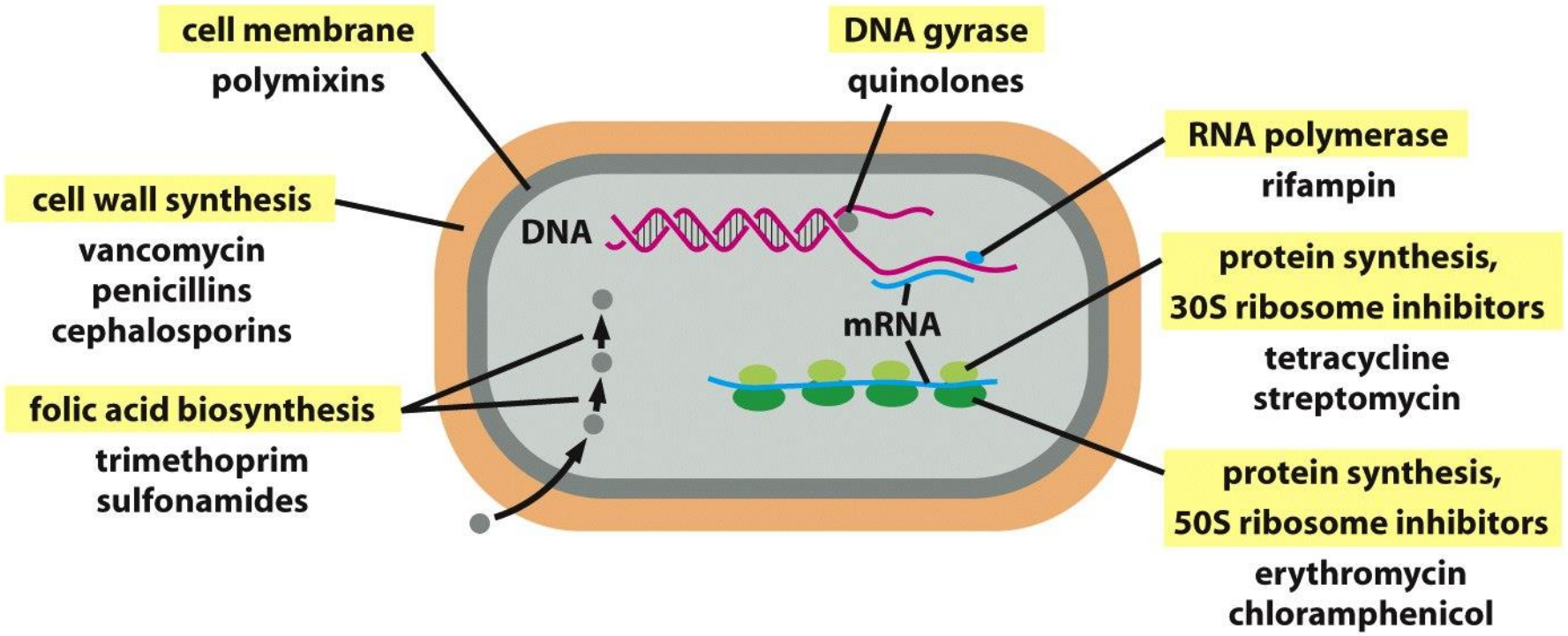


Figure 24-44 *Molecular Biology of the Cell* (© Garland Science 2008)

Antibiotic resistance

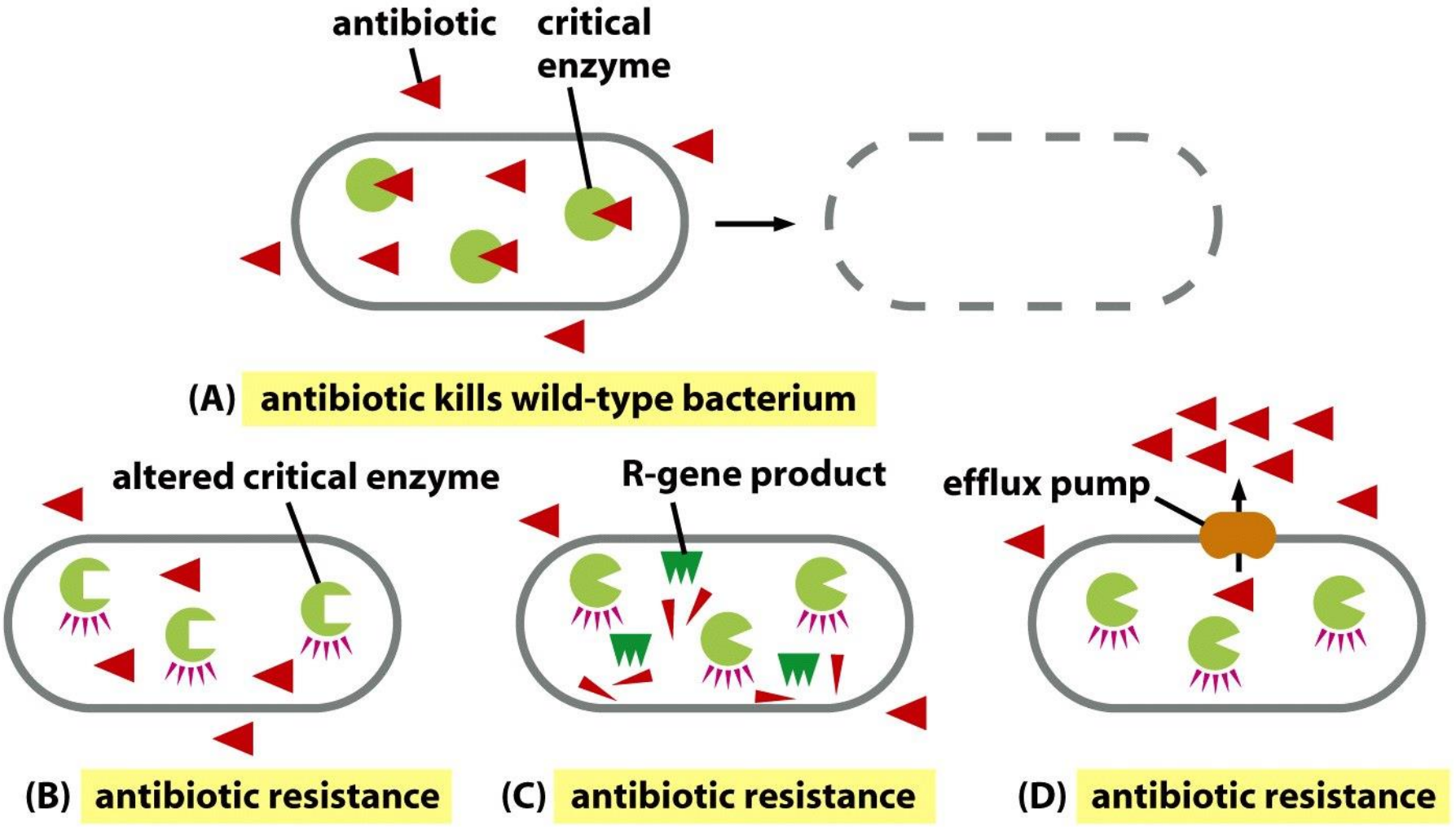


Figure 24-45 *Molecular Biology of the Cell* (© Garland Science 2008)

Listeria hijacks host actin

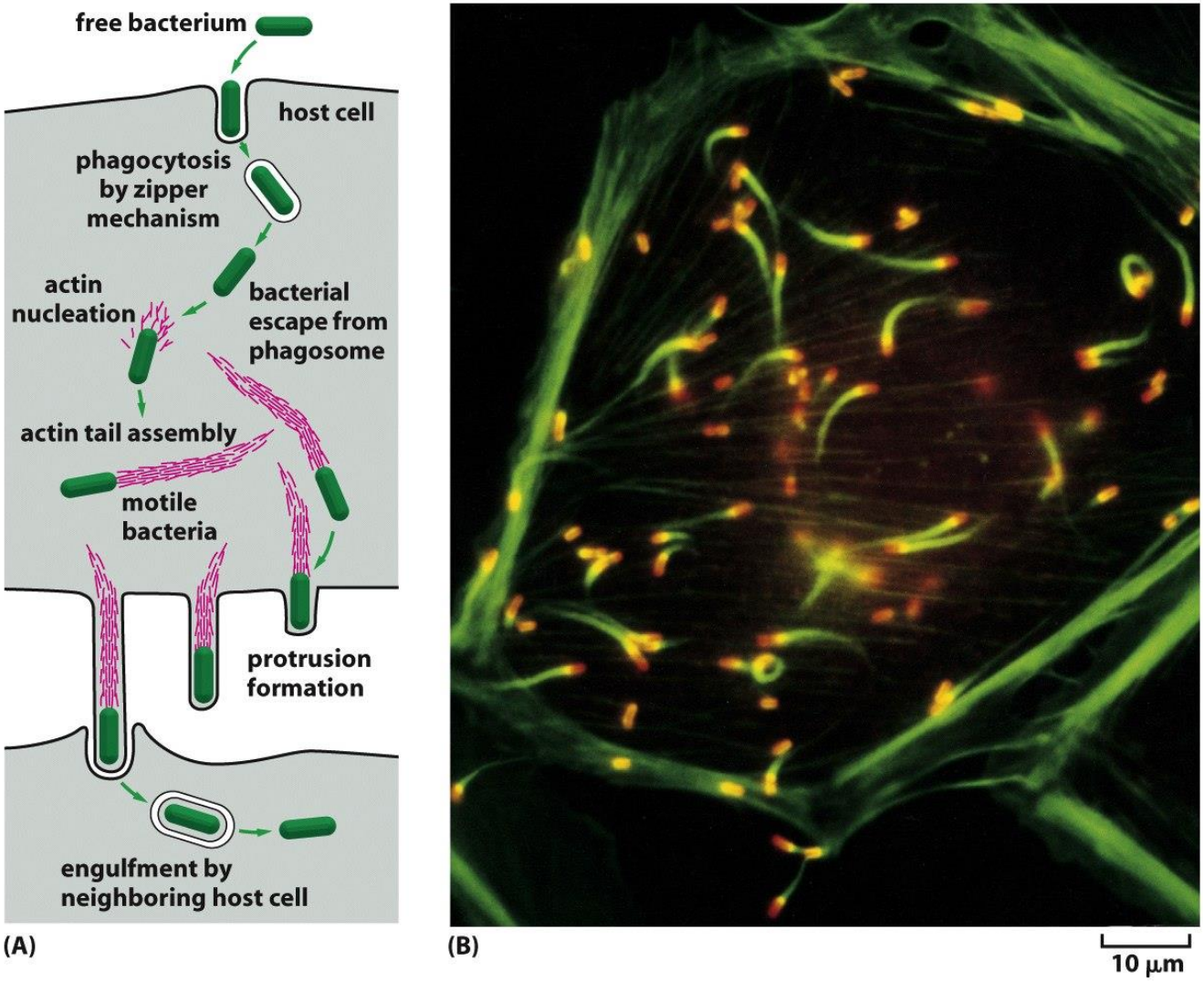
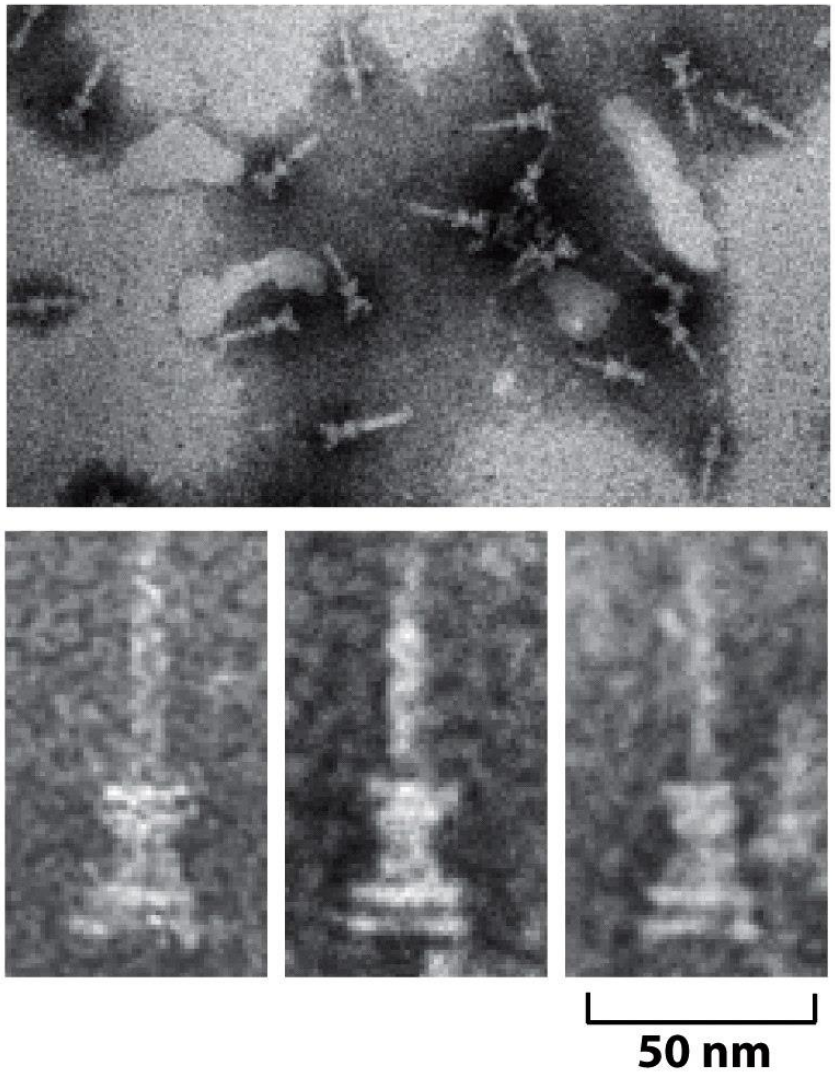


Figure 24-37 *Molecular Biology of the Cell* (© Garland Science 2008)

Methicillin Resistant Staphylococcus aureus (MRSA)

- **Group of Gram positive bacterial strains**
- ***S. aureus***
  - Colonizes skin and moist squamous epithelium of the anterior nares (nasal)
    - 20% colonized, 60% intermittent carriers, 20% don't have it
  - Can infect through skin abrasions, abscesses, burns or surgical sites
- **Generally a limited cause of pneumonia in the public**
  - Hospital acquired infection (HA-MRSA) is more associated with pneumonia
    - Ventilator associated pneumonia
- **MRSA - Highly resistant to methicillin class of antimicrobials**
  - Misnomer since this class of antibiotics is not used to treat this pathogen (within the last 10 years)

Type III secretion system



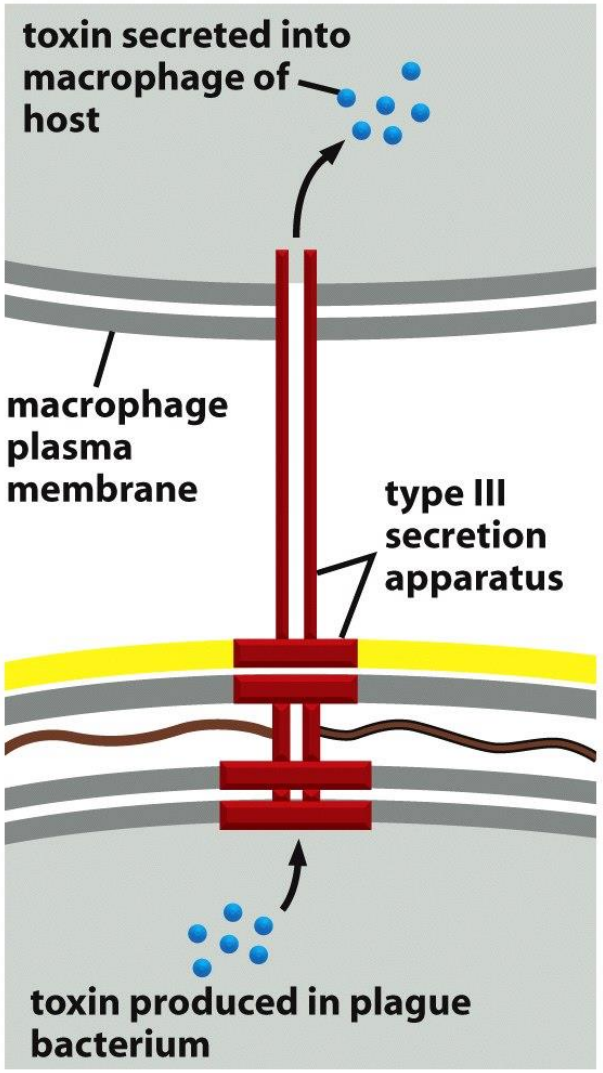


Figure 24-8a *Molecular Biology of the Cell* (© Garland Science 2008)

Attaching and Effacing

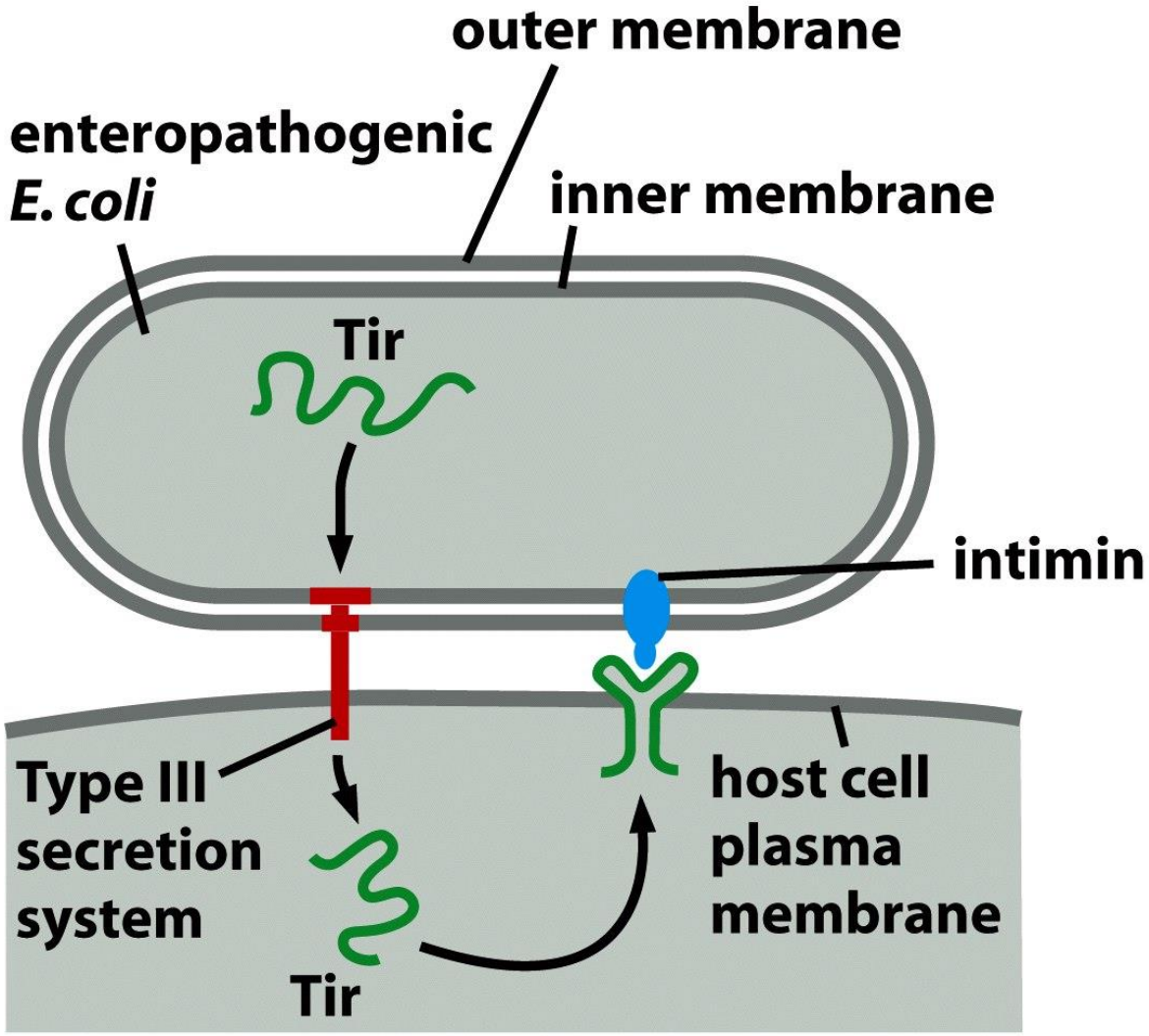


Figure 24-22a *Molecular Biology of the Cell* (© Garland Science 2008)

Attaching and Effacing

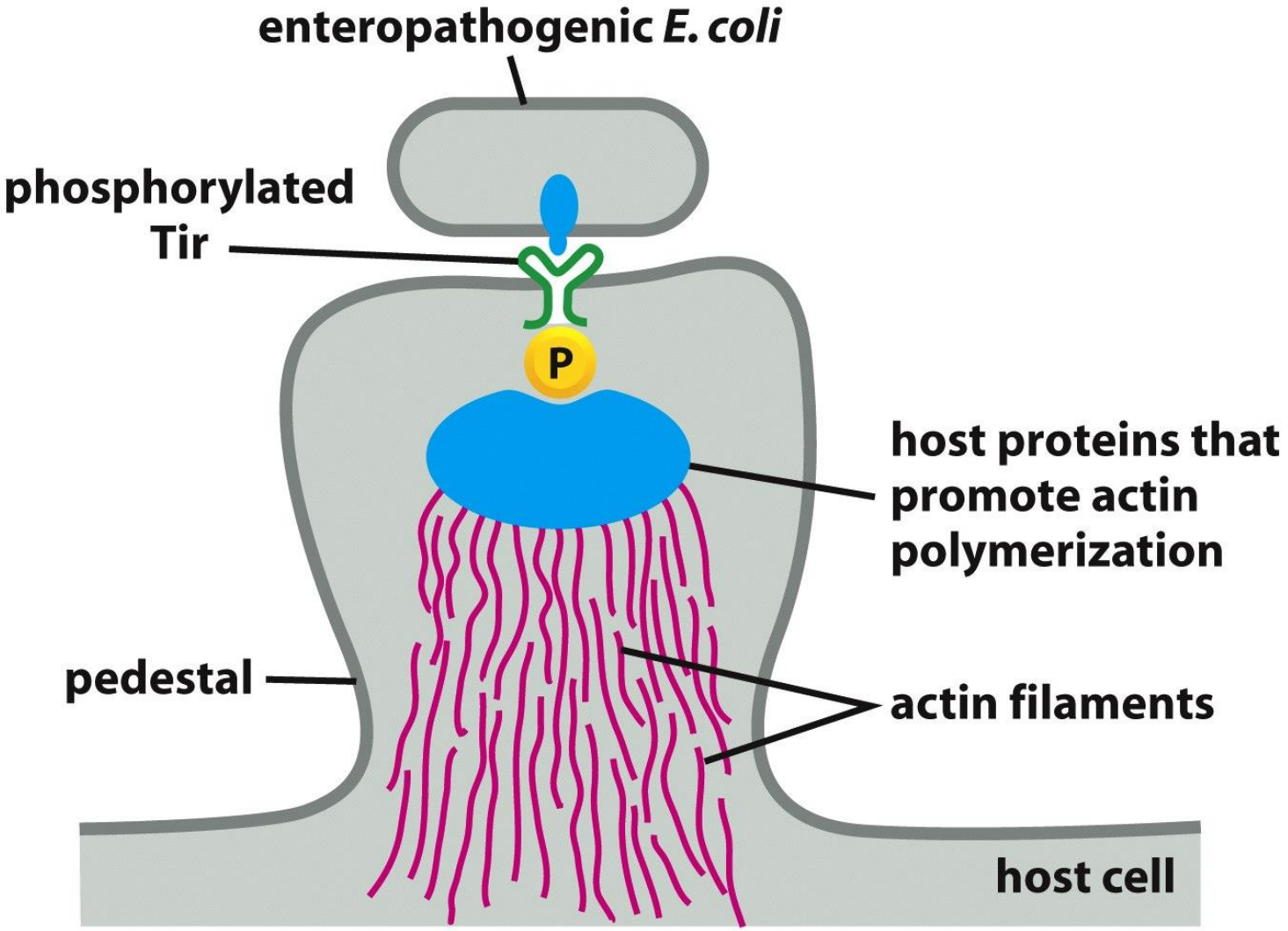


Figure 24-22b *Molecular Biology of the Cell* (© Garland Science 2008)

Attaching and Effacing

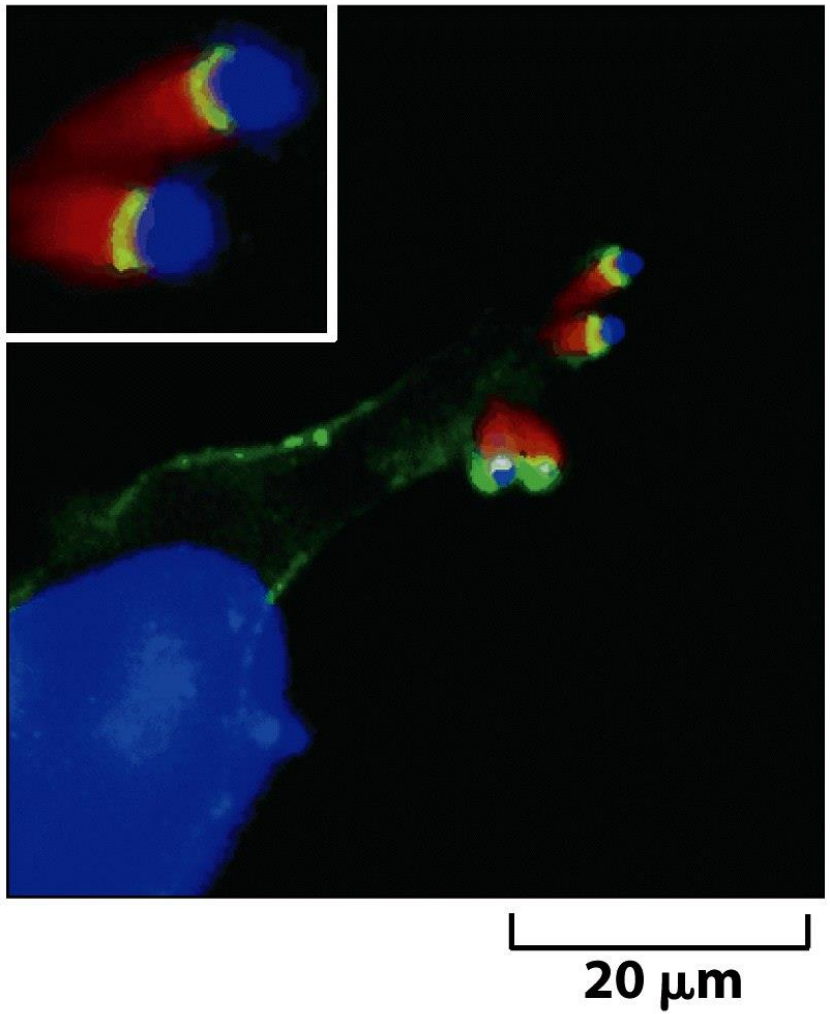
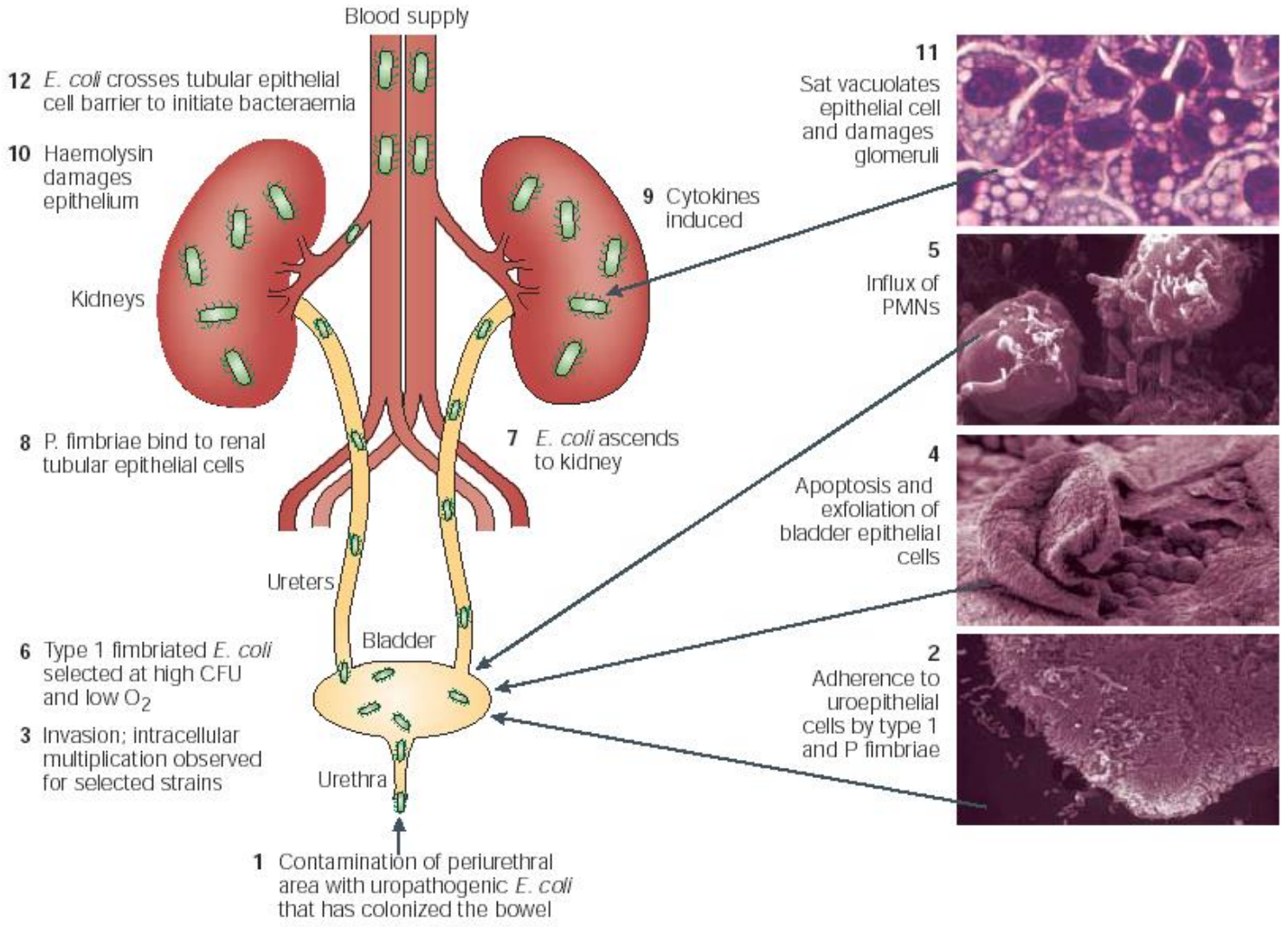


Figure 24-22c *Molecular Biology of the Cell* (© Garland Science 2008)

Uropathogenic *E. coli* (UPEC)



MINES Saint-Étienne

Pathogen types: virus

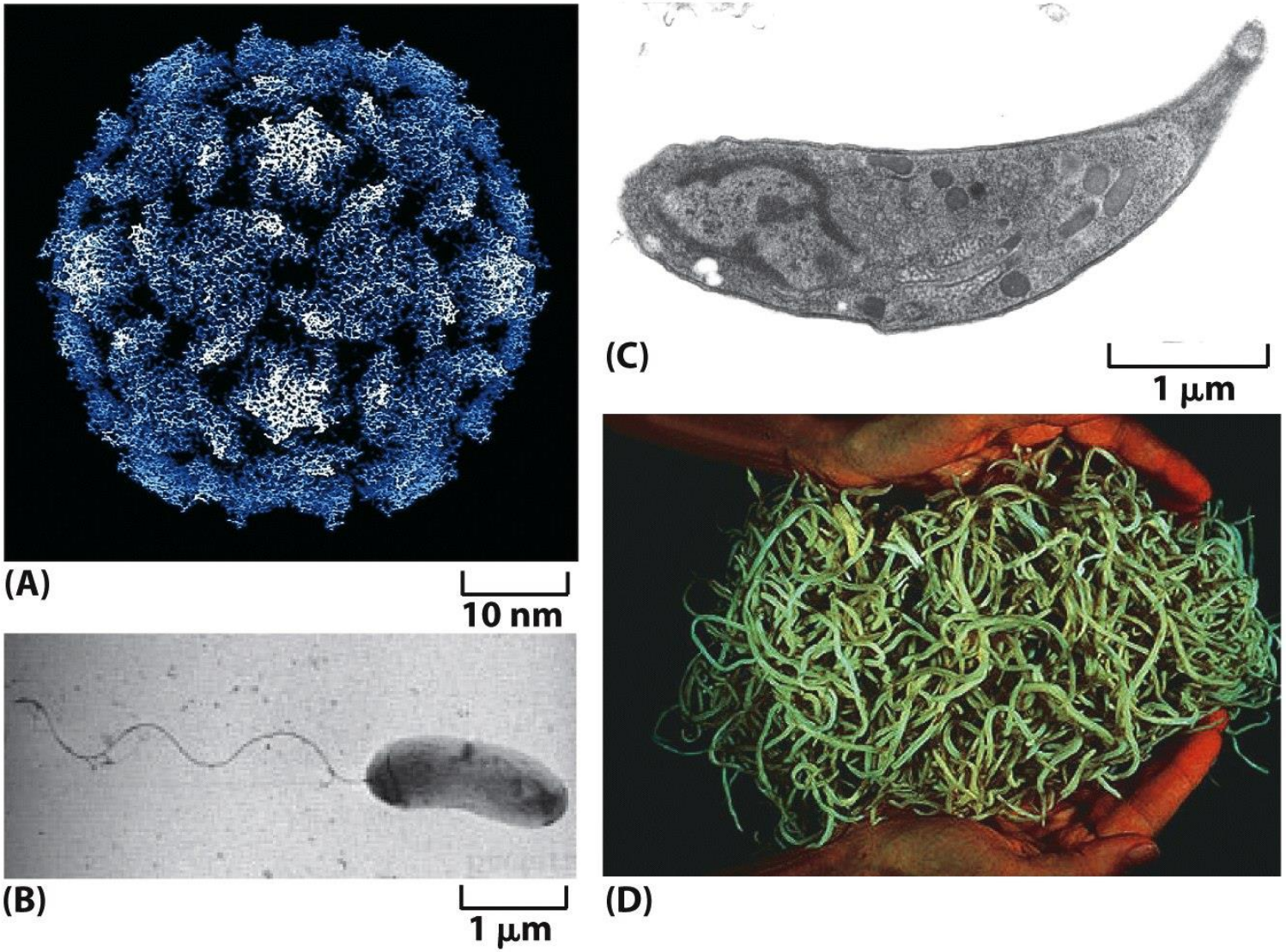


Figure 24-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Viruses (poliovirus)

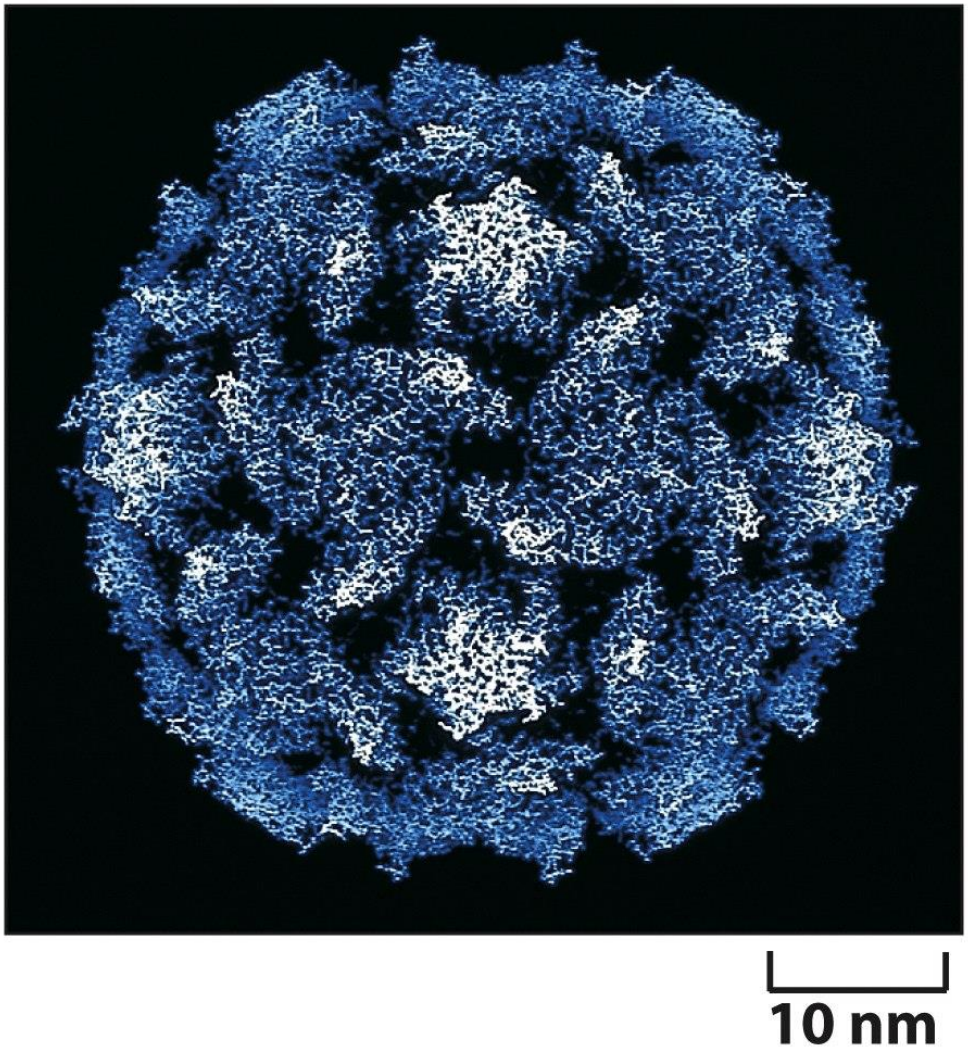
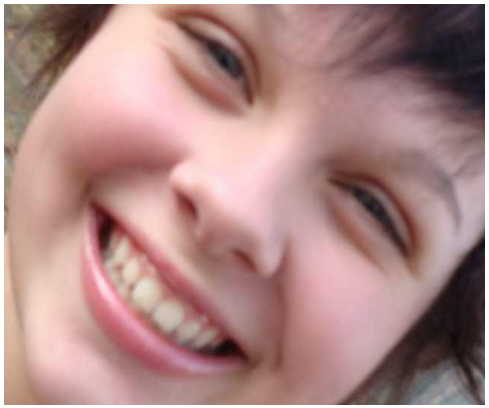


Figure 24-3a *Molecular Biology of the Cell* (© Garland Science 2008)

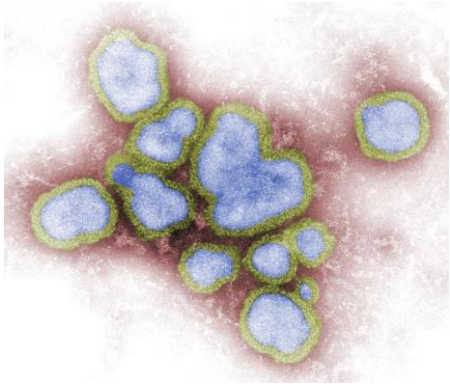
How Do Viruses Differ From Living Organisms?

- **Viruses are not living organisms because they are incapable of carrying out all life processes.**



Living Multicellular Organism: Kayla

- **Viruses**
  - are not made of cells
  - can not reproduce on their own
  - do not grow or undergo division
  - do not transform energy
  - lack machinery for protein synthesis



Nonliving / Acellular Infectious Agent: H1N1 Influenza Virus

Images: H1N1 Influenza Virus, Public Health Image Library PHIL #11702

Table 13.1 The Novel Properties of Viruses

Viruses	Cells
Are inert macromolecules outside of a cell, but become active inside a cell	Metabolize on their own
Do not divide or grow	Divide and grow
Acellular	Cellular
Obligate intracellular parasites	Most free-living
Contain either DNA or RNA, never both	Contain both DNA and RNA
Genome can be dsDNA, ssDNA, dsRNA, or ssRNA	Genome is dsDNA
Ultramicroscopic in size, ranging from 10 nm to 300 nm	300 nm to 12 cm in diameter
Have a proteinaceous capsid around genome; some have an envelope around the capsid	Surrounded by a phospholipid membrane and often a cell wall
Replicate in an assembly-line manner using the enzymes and organelles of a host cell	Self-replicating by asexual and/or sexual means

What Are Viruses Made Of?

- Nucleic acid, proteins, and sometimes, lipids.
- Nucleic acid surrounded by a protective protein coat, called a capsid
- An outer membranous layer, called an envelope made of lipid and protein, surrounds the capsid in some viruses.

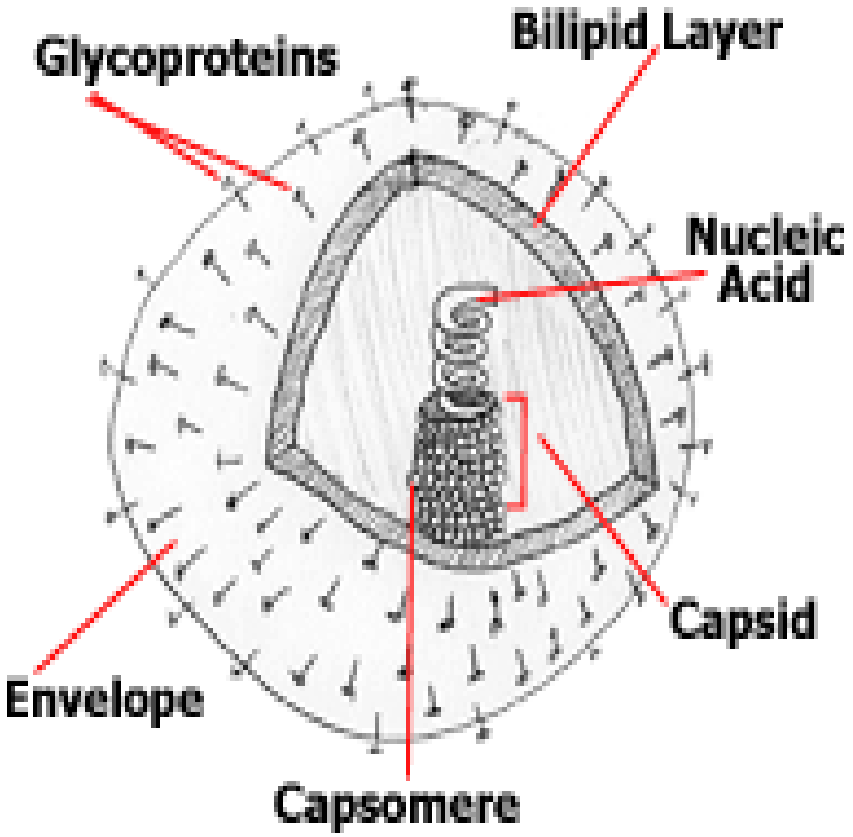


Image: Virus Structure : www.peteducation.com

What Are Viruses Made Of?

Capsid Morphology

- **Protein coat provides protection for viral nucleic acid and means of attachment to host's cells.**
- **Composed of proteinaceous subunits called capsomeres.**
- **Some capsids composed of single type of capsomere; others composed of multiple types.**

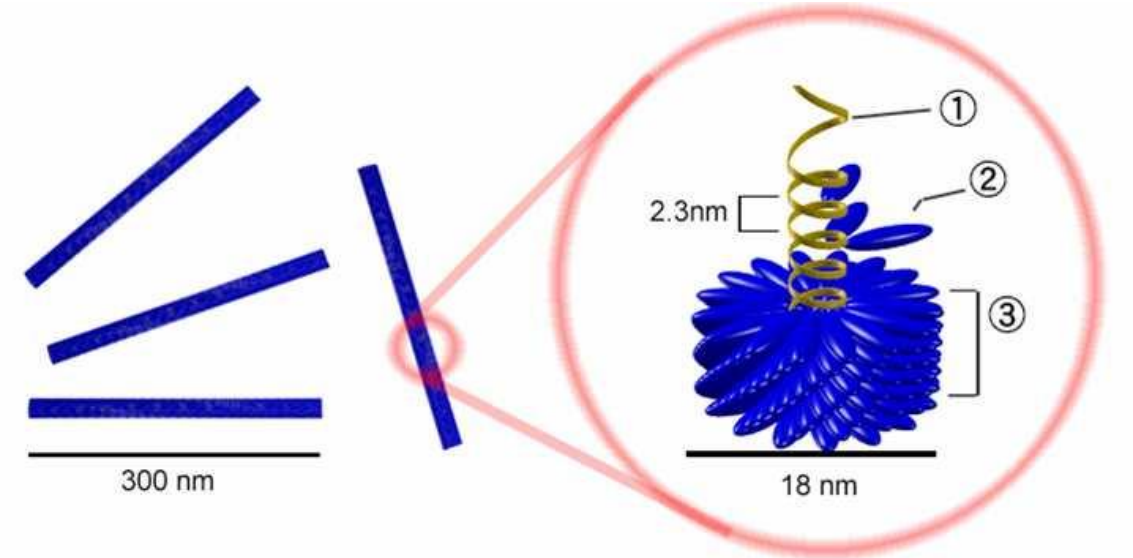


Image: Tobacco Mosaic Virus Structure, Graham Colm, wiki

How Are Viruses Classified?

- DNA viruses contain DNA as their genetic material.
- RNA viruses contain RNA as their genetic material.

- Helical – capsomeres bonded, spiral shape
- Polyhedral – flat sides
- Spherical - round
- Complex – many different shapes

- **Presence or absence of a membranous envelope surrounding the capsid.**
- **Kinds of host they attack**
  - Bacteriophage
  - Animal Viruses

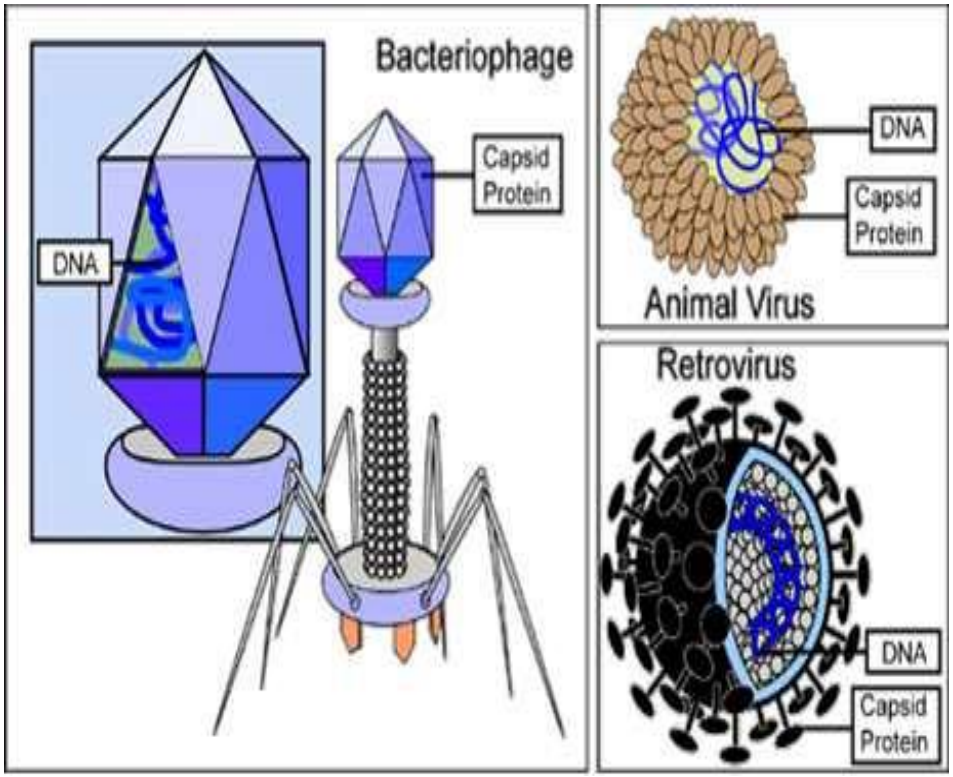


Image: Types of Viruses, National Institutes of Health

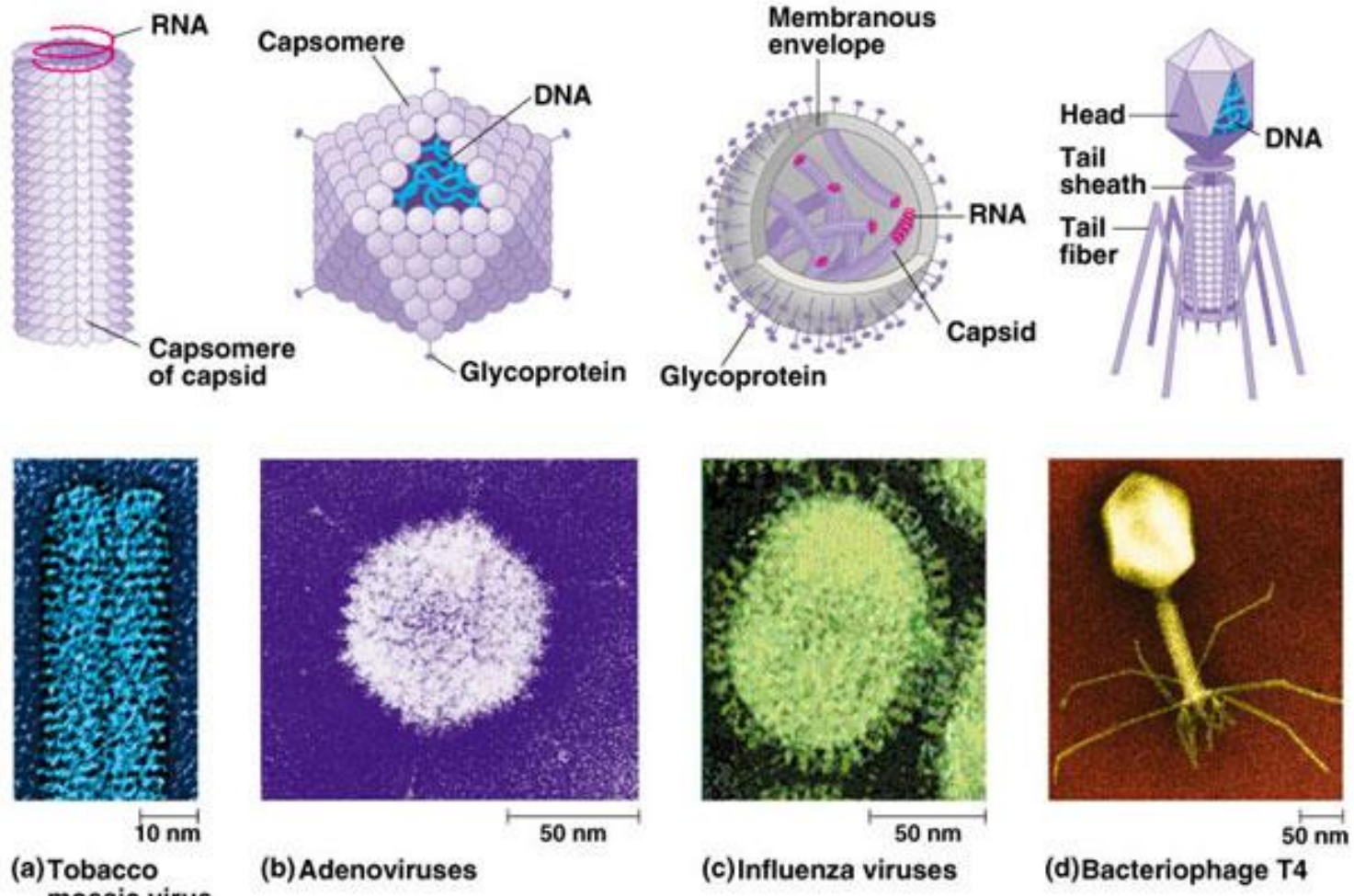
Shapes of Viruses

Helical

Polyhedral

Spherical

Bacteriophage



Shapes of Viruses

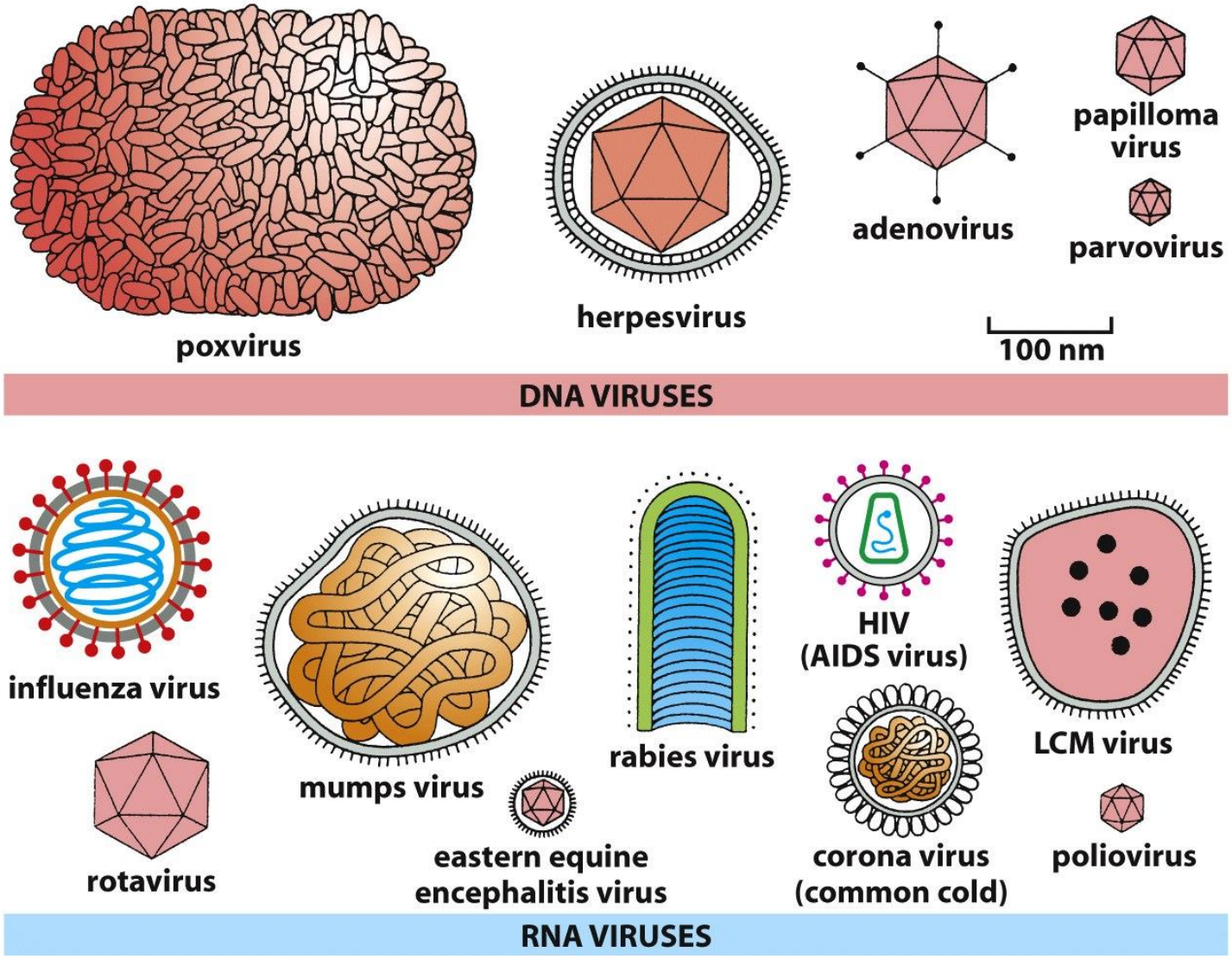
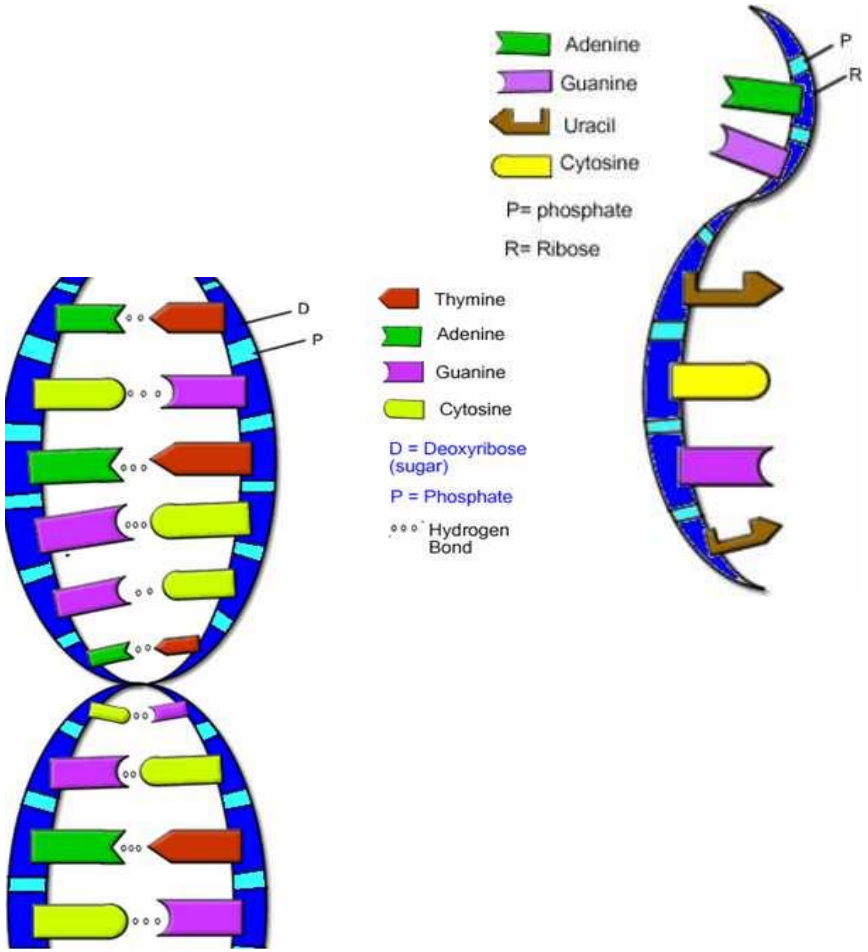


Figure 24-13 *Molecular Biology of the Cell* (© Garland Science 2008)

Genetic Material of Viruses

- Show more variety in nature of their genomes than do cells
- Can be DNA or RNA; never both
- Primary way scientists categorize and classify viruses
- Can be dsDNA, ssDNA, dsRNA, ssRNA
- May be linear and composed of several segments or single and circular
- Much smaller than genomes of cells



Images: DNA & RNA Diagram, BiologyCorner.com

Viral DNA

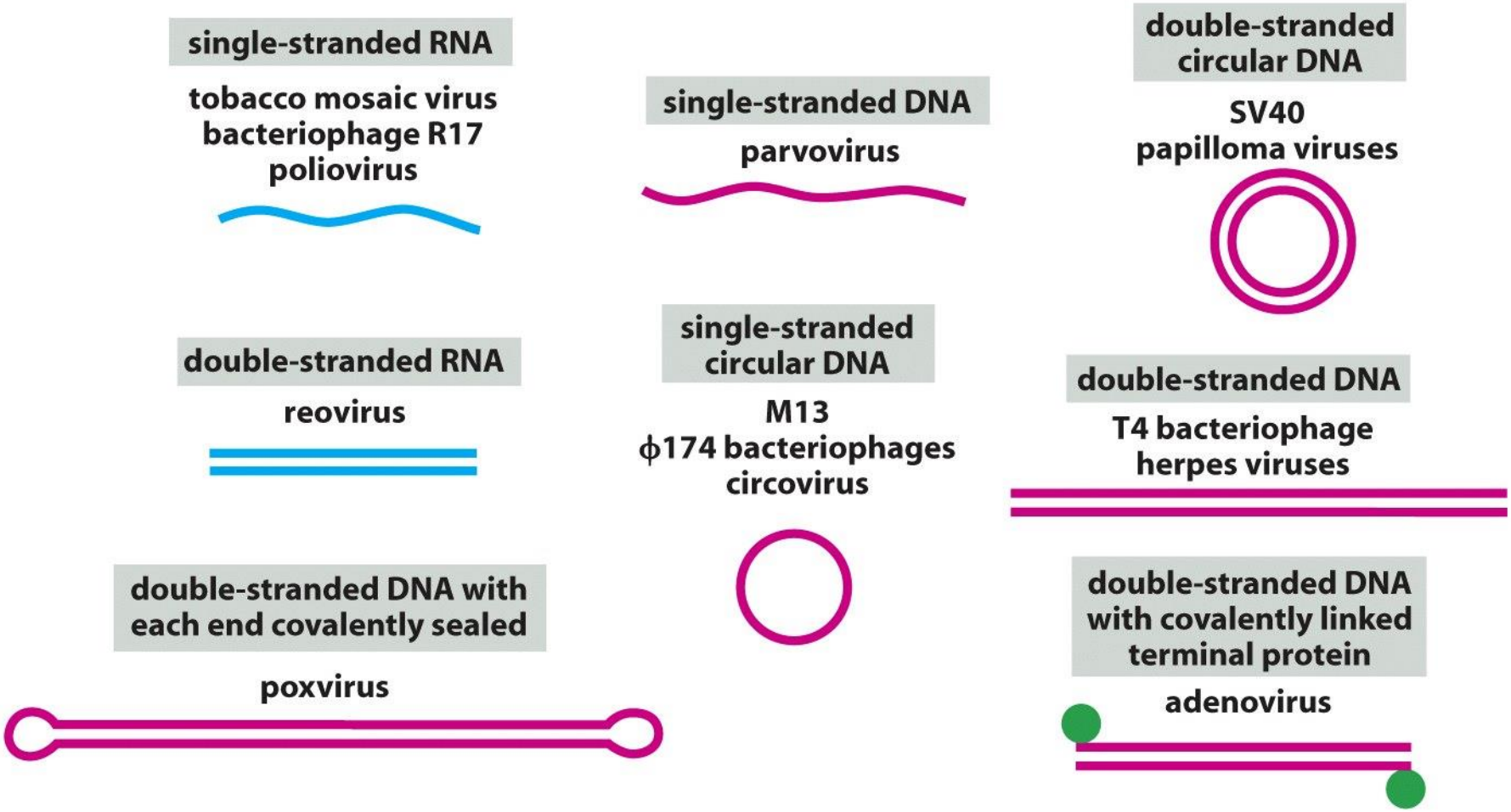


Figure 24-14 *Molecular Biology of the Cell* (© Garland Science 2008)

The Viral Envelope

- Acquired from host cell during viral replication or release; envelope is portion of membrane system of host.
- Composed of sugars and proteins; some proteins are virally-coded glycoproteins (spikes).
- Envelope's proteins and glycoproteins often play role in host recognition.

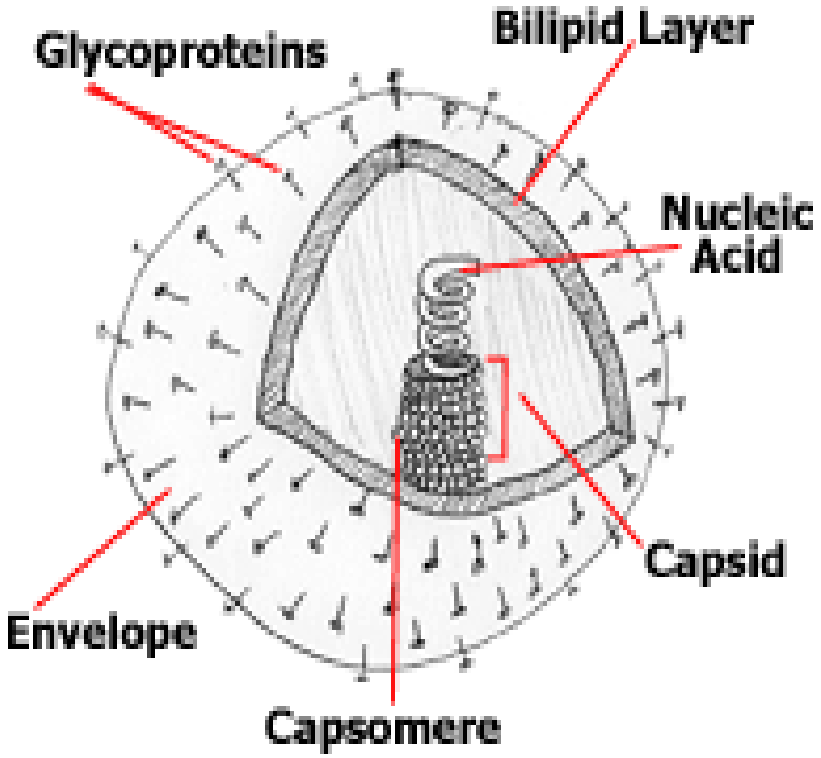
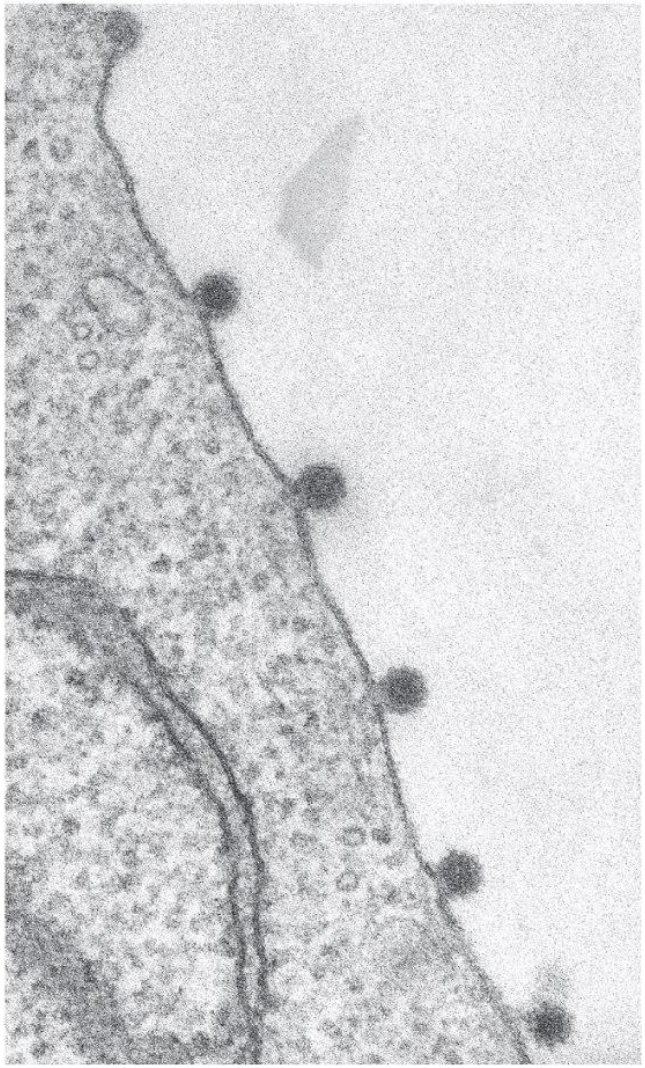


Image: Virus Structure : www.peteducation.com

Viral envelope



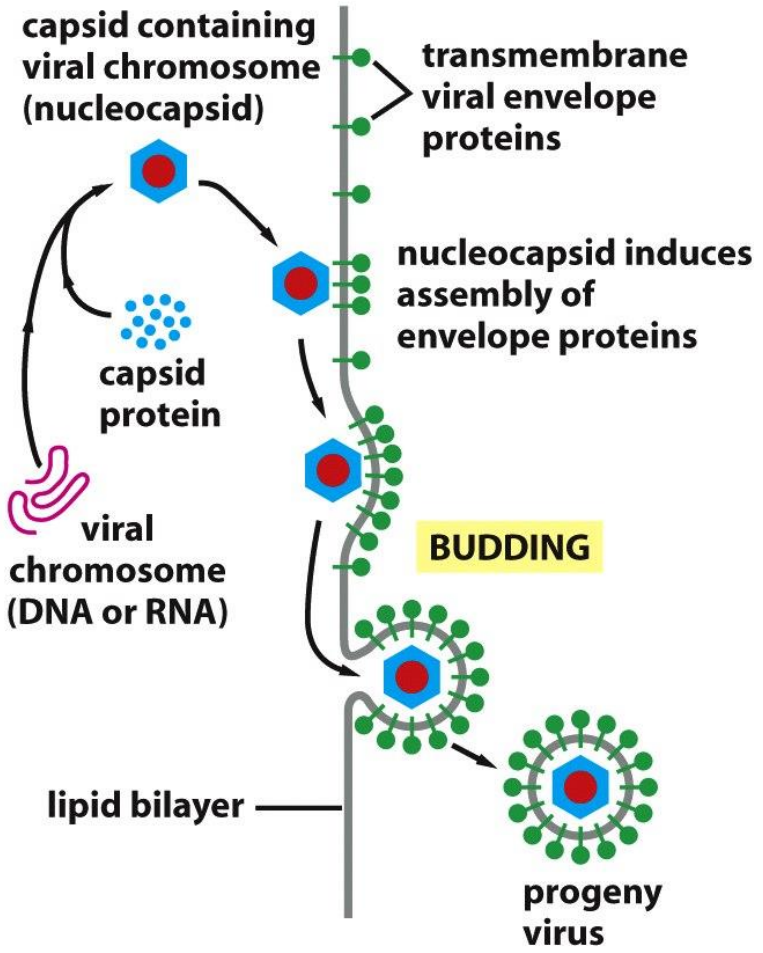


Figure 24-15 *Molecular Biology of the Cell* (© Garland Science 2008)

HIV genome

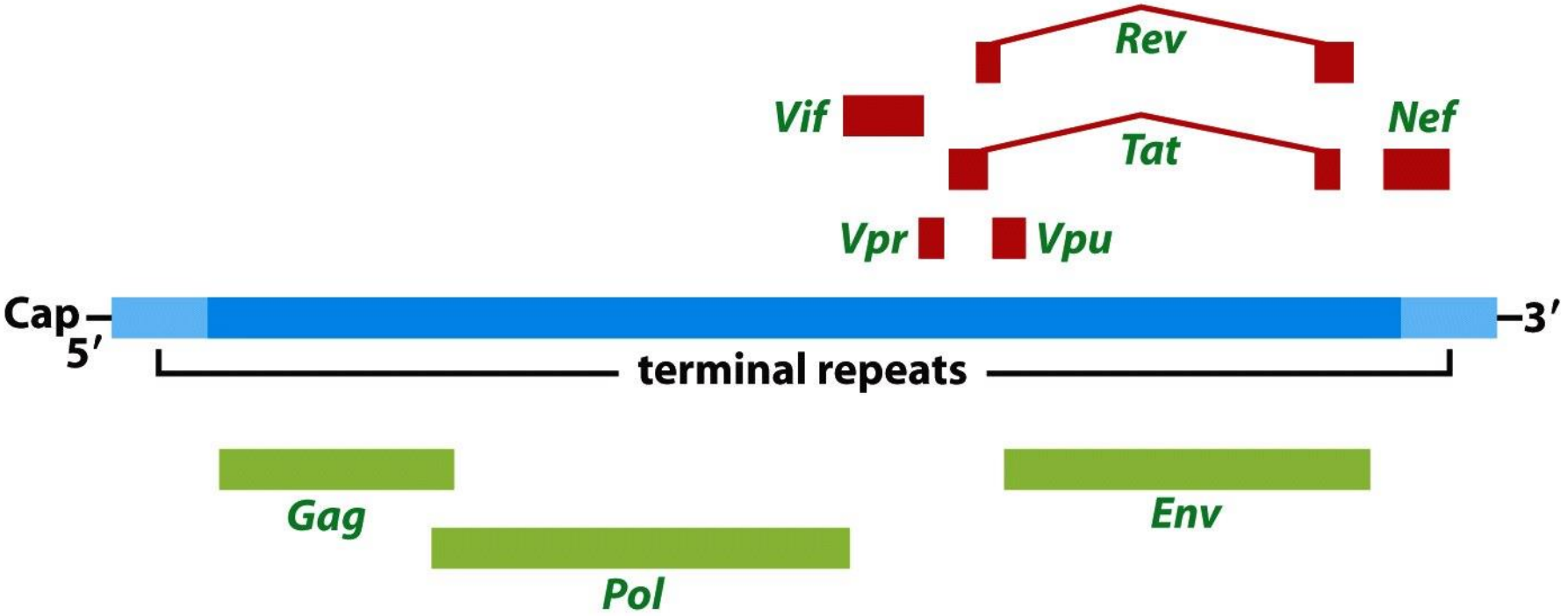
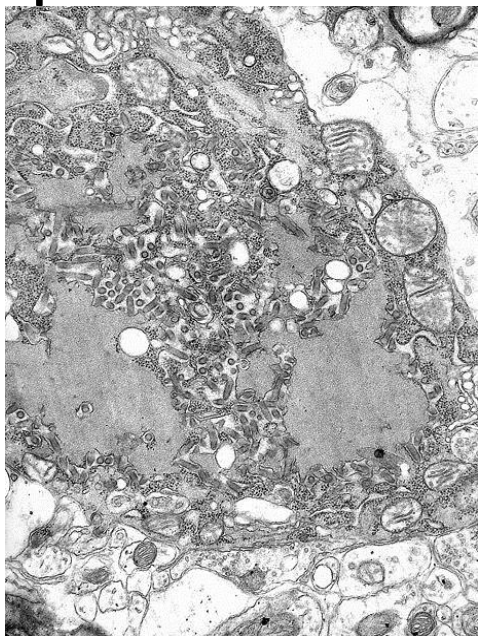


Figure 24-16 *Molecular Biology of the Cell* (© Garland Science 2008)

Systematic Classification of Viruses

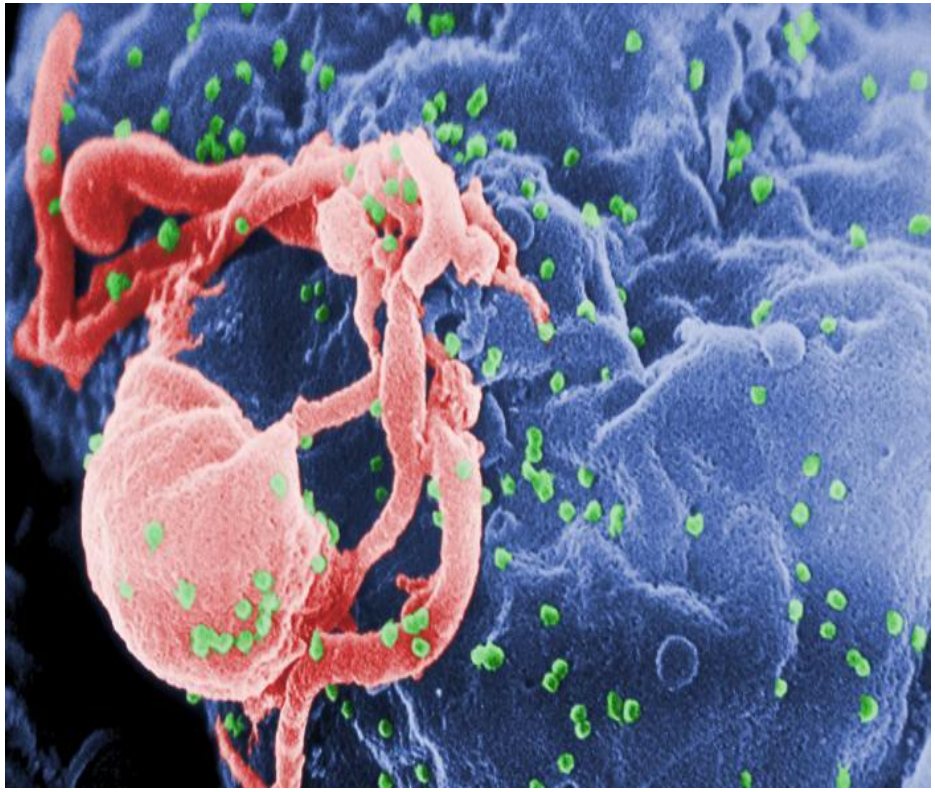
- International Committee on Taxonomy of Viruses established 1966 to provide a single taxonomic scheme for viral classification.
- Viruses categorized by type of nucleic acid, presence or absence of an envelope, shape and size.
- For most viruses, Families are the highest taxonomic group.
- At this time, Latinized names are not given to viruses at the species level.

	HIV	Rabies
Order:	**----**	**Mononegavirale**
Family:	**Retroviridae**	**Rhabdoviridae**
Genus:	***Lentivirus***	***Lisavirus***
Species:	**Human-immunodeficiency virus**	**Rabies virus**



Micrograph with numerous rabies virions (small dark-grey rod-like particles). Public health Image Library, Dr. Fred Murphy

How Does a Virus Infect Its Host?



Human Immunodeficiency Virus (HIV)

(Depicted in green, budding off infected white blood cell.)

Images: HIV viruses budding off of infected lymphocyte, PHIL #10000

Virus lifecycle

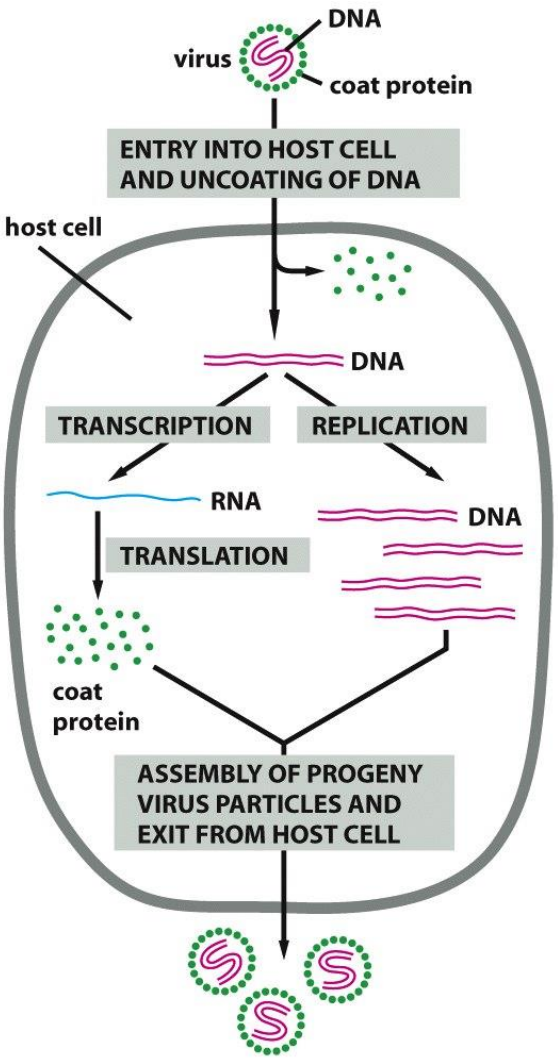
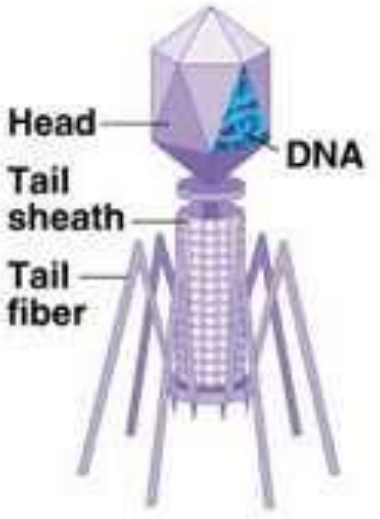
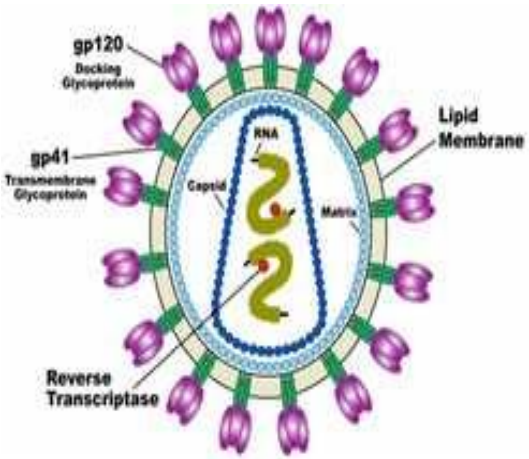


Figure 24-12 *Molecular Biology of the Cell* (© Garland Science 2008)

How Does a Virus Infect Its Host?

- **Most viruses infect only a certain type of host.**
- **Specificity due to affinity of viral surface proteins/glycoproteins to proteins/glycoproteins on the surface of the host cell.**
- **Bacteriophages have proteins in their tail fibers *(those extensions that look like legs)* that attract to proteins on the surface of bacterial cells.**
- **Most viruses have proteins or glycoprotein spikes that correspond to glycoproteins on the surface of animal cells.**
- **Viruses may also be so specific that they infect a particular cell of the host organism. *(HIV only attacks helper-T lymphocytes, a type of white blood cell, in humans)***





Images: Bacteriophage, Pearson Education, HIV Virion, National Institutes of Health.

HIV receptors

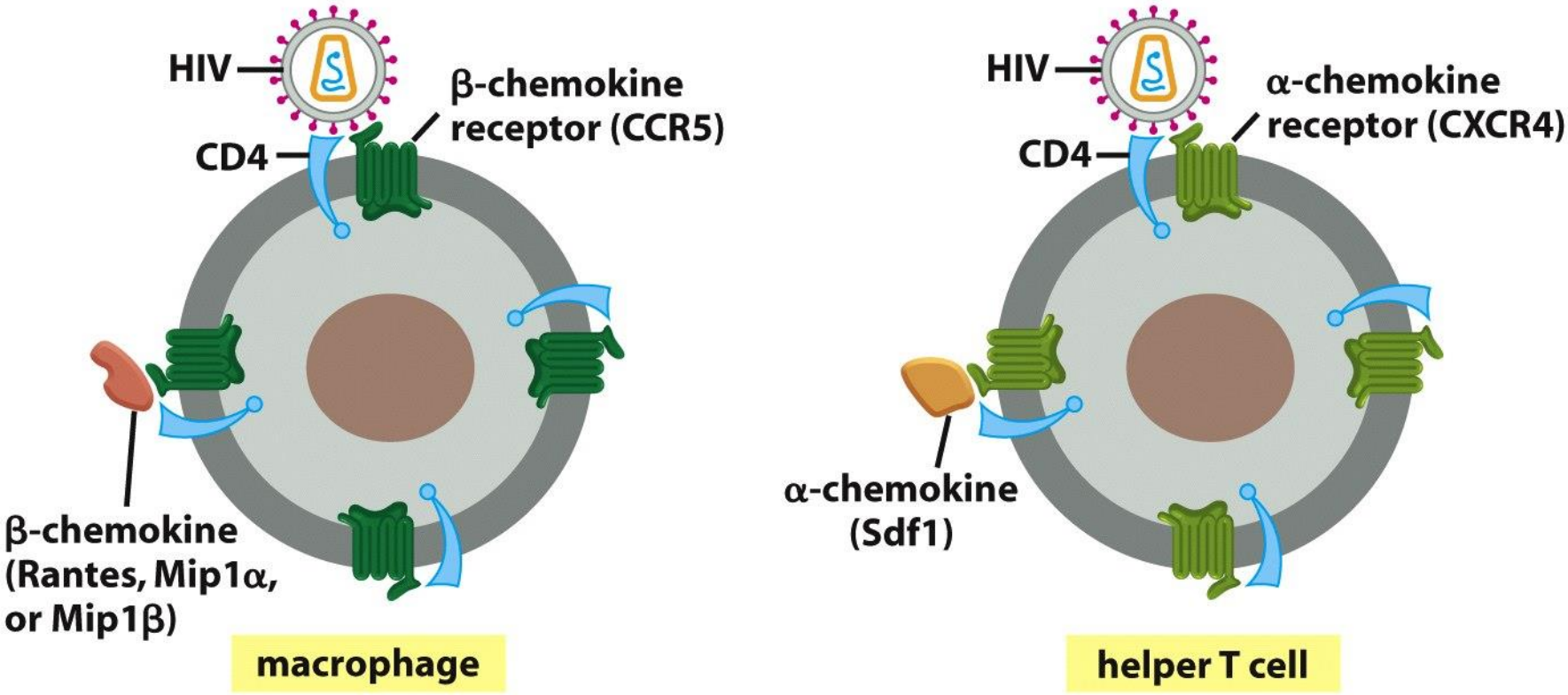


Figure 24-23 *Molecular Biology of the Cell* (© Garland Science 2008)

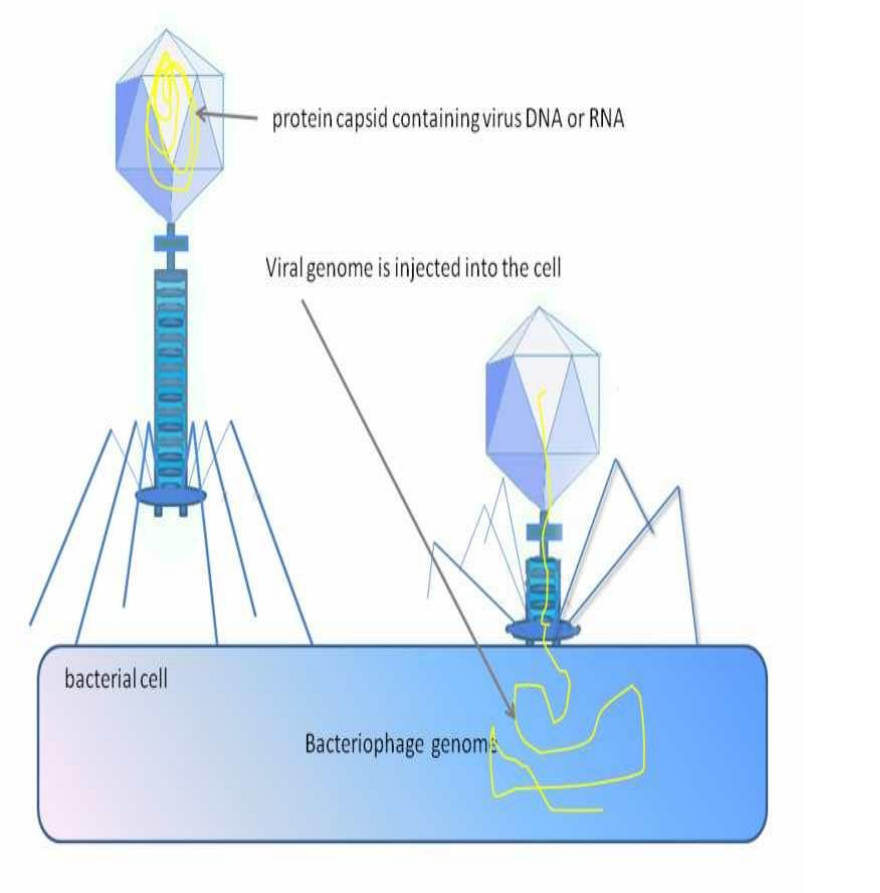
A virus must get inside its host cell to infect it

Extracellular state

- Called virion *(vie-ree-on)*
- Protein coat (capsid) surrounding nucleic acid
- Some have phospholipid envelope
- Outermost layer provides protection and recognition sites for host cells

Intracellular state

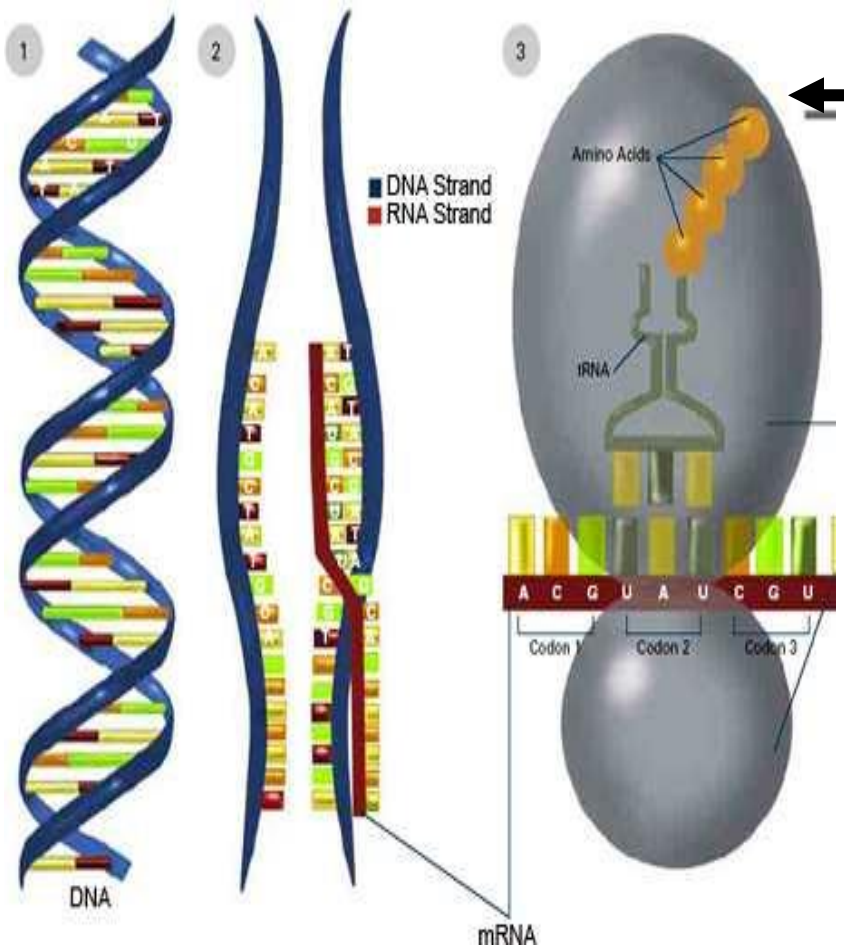
- Capsid removed
- Virus exists as nucleic acid (genetic material)



Bacteriophage injecting DNA into bacterial cell

How Do Viruses Reproduce?

Nucleic acids (DNA & RNA) are blueprints; instructions for building proteins.



Protein being built from amino acid building blocks.

Image: Transcription Translation, National Institute of General Medical Sciences

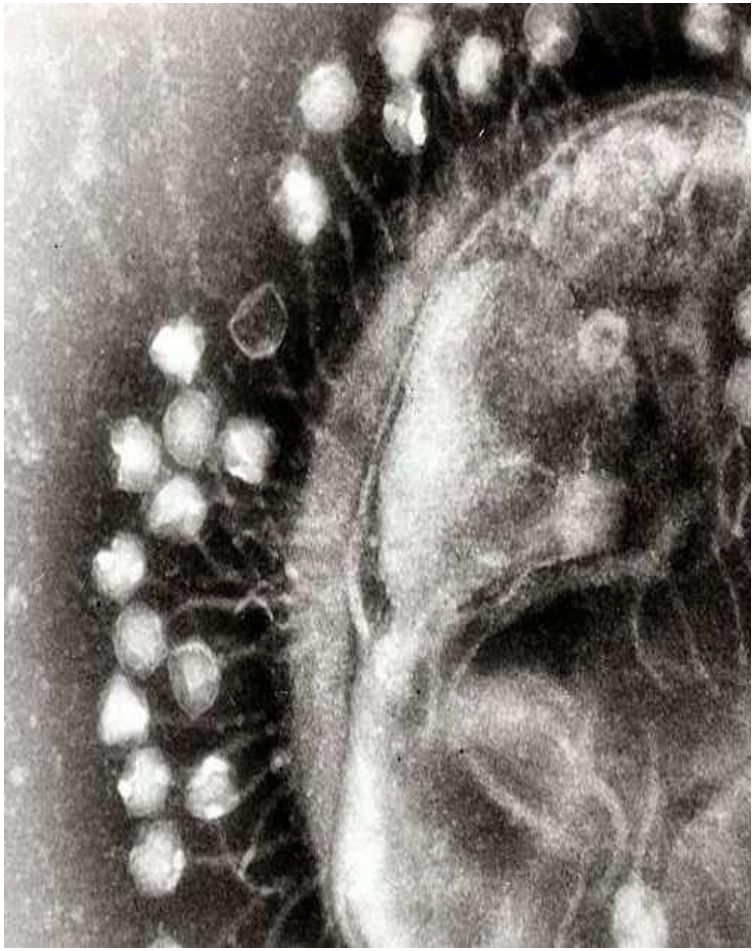
Viruses make more viruses by:

1. inserting their genetic material into a host cell
2. having the cell read the viral genetic instructions and manufacture the raw materials to build copies of the virus
   - cell makes copies of the viral genetic instructions
   - cell makes viral proteins from the viral genetic instructions
3. The viral parts and pieces self-assemble and then exit the host cell.

How does flu virus infect?
http://www.youtube.com/watch?v=Rpj0emEGShQ

Bacteriophages

Phages are Viruses That Infect Bacteria



Images: [Bacteriophage viruses infecting a bacterium](), Graham Colm, Public Domain, Wiki

Bacteriophage lifecycle

A bacteriophage is a virus that attacks and destroys bacterial cells.

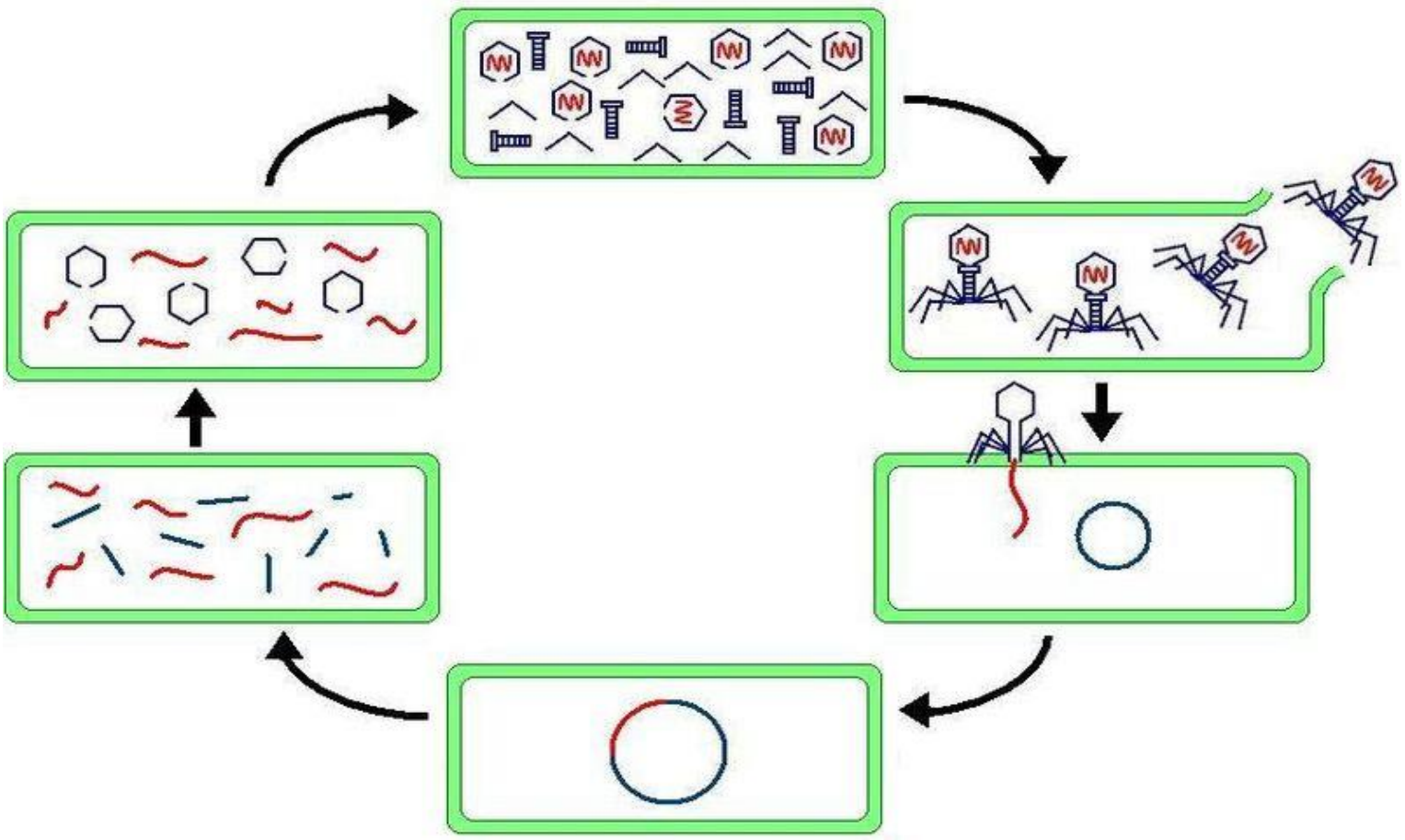


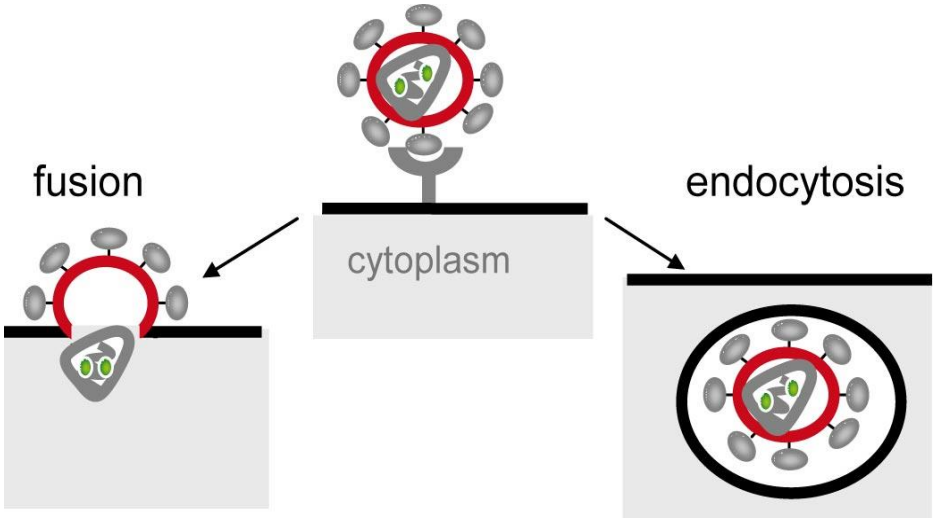
*Image: **Bacteriophage Lytic Replication**, Suly12 Wikimedia Commons*

How Do Viruses enter animal cells

Not completely understood, but appears to be 3 methods:

- Direct penetration of naked virus
  - *Viral genome enters cell, while capsid remains on cell's surface. Like how phages enter bacteria.*
- Membrane fusion
- Endocytosis

  With membrane fusion and endoocytosis, the capsid is removed once inside the host cell.



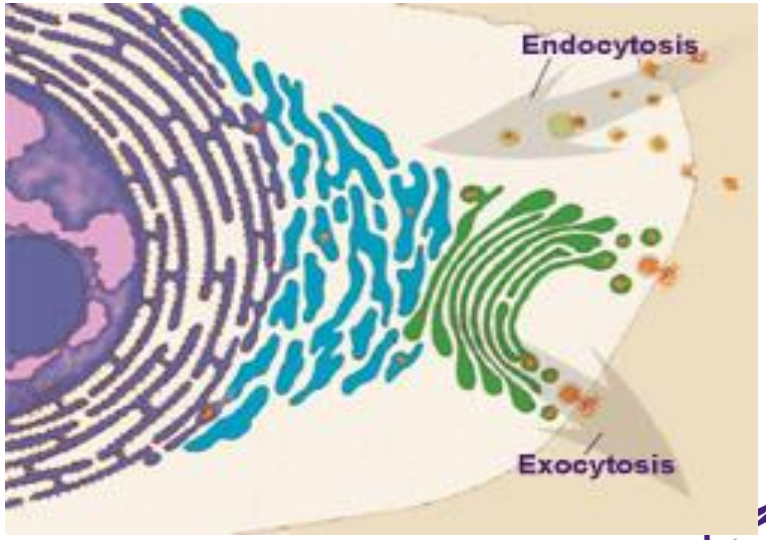


Image: Virus Entry into Cell; Endocytosis & Exocytosis, NIGMS

Uncoating strategies

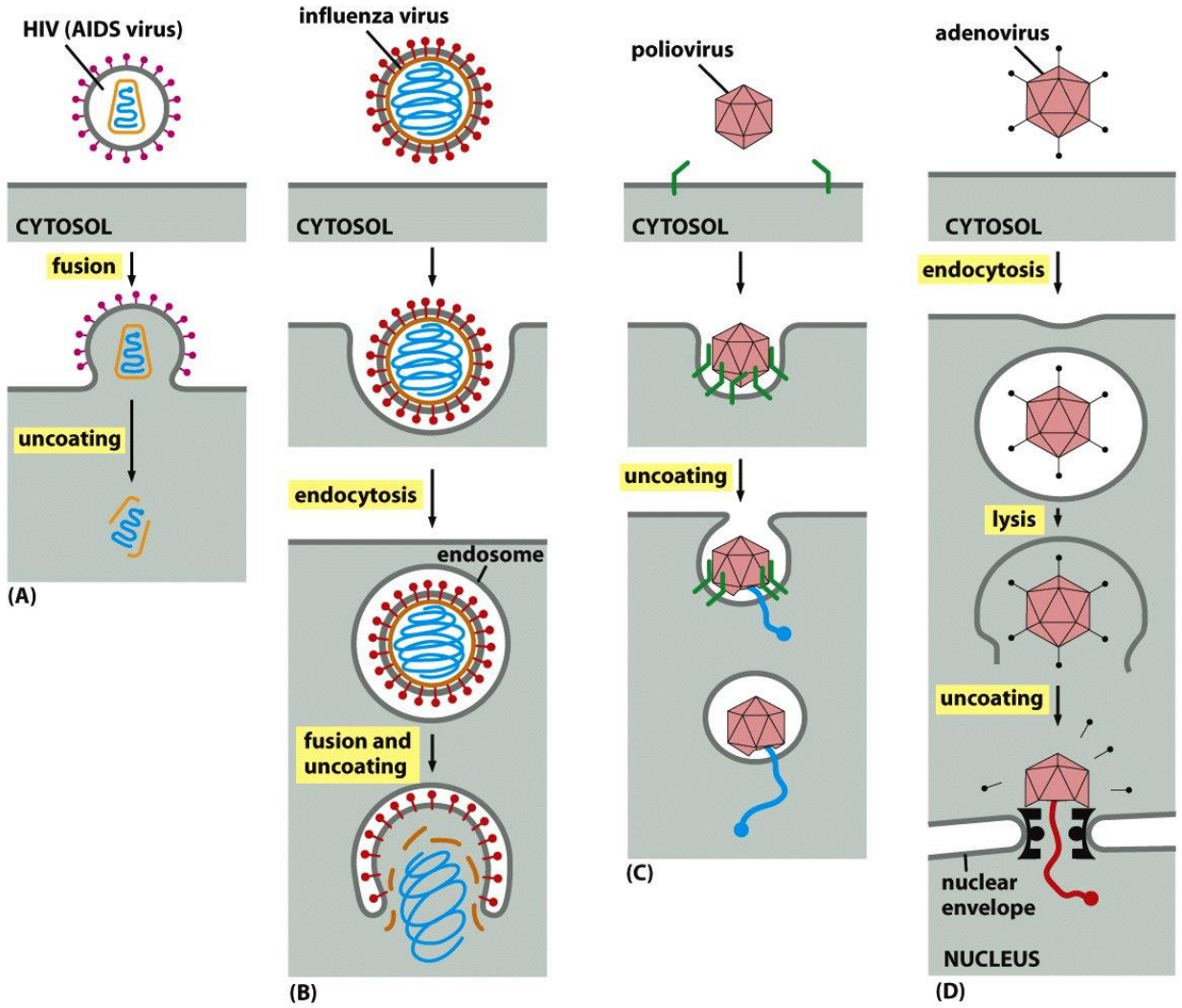
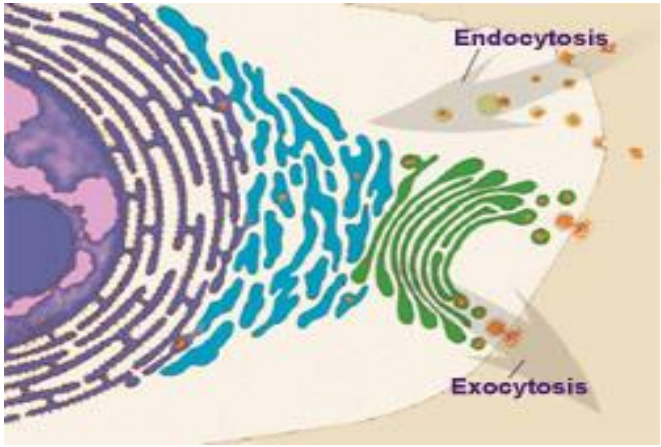


Figure 24-24 *Molecular Biology of the Cell* (© Garland Science 2008)

How Do Viruses exit animal cells

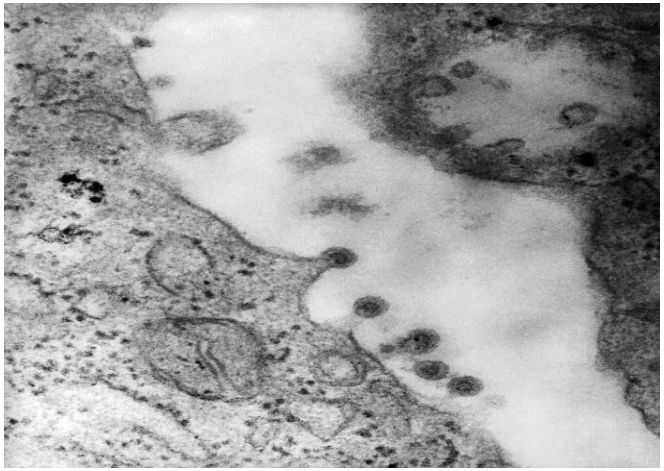
_____ viruses

After construction of capsid, naked viruses ,may be released from the animal cell through exocytosis or may cause lysis and death of the cell.



_____ viruses

Often released through a process called *budding*. Virus exits cell with part of the cells membrane.



Endocytosis / Exocytosis Animation:
http://www.phschool.com/science/biology_place/biocoach/biomembrane2/cytosis.html

Images: Endocytosis & Exocytosis, NIGMS; Rubella virions budding, PHIL # 10220

Herpes virus coating

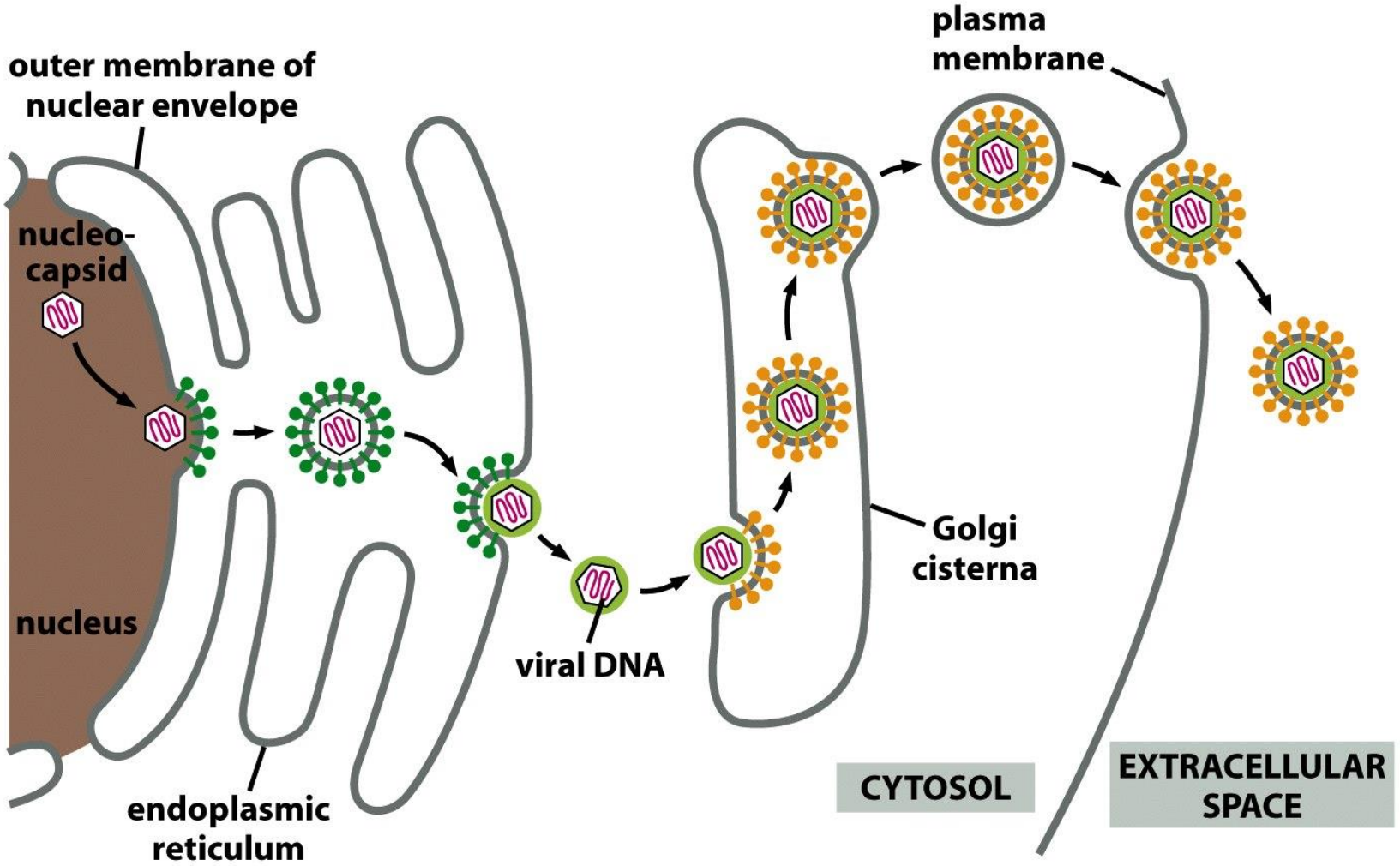


Figure 24-35a *Molecular Biology of the Cell* (© Garland Science 2008)

Vaccinia virus coating

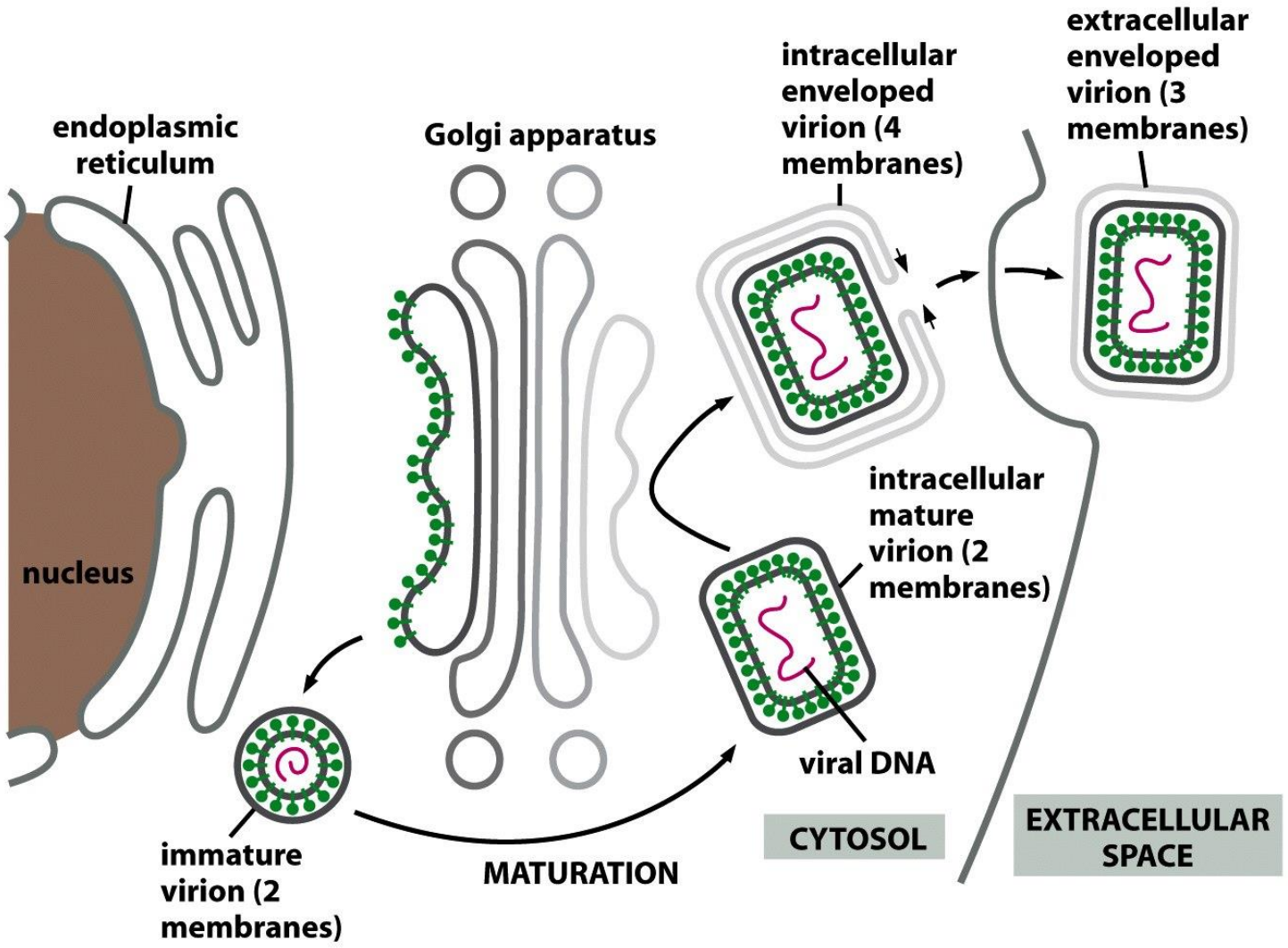


Figure 24-35b *Molecular Biology of the Cell* (© Garland Science 2008)

Vaccinia virus actin remodelling

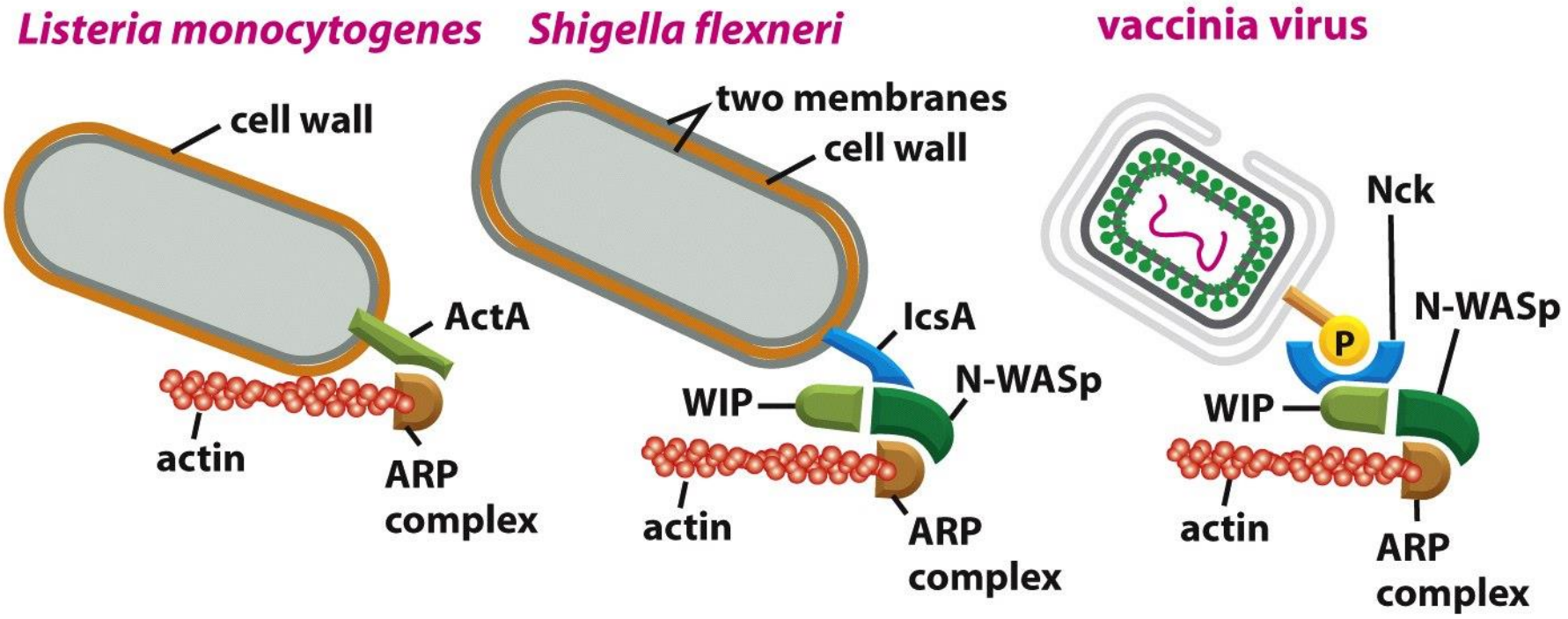


Figure 24-38 *Molecular Biology of the Cell* (© Garland Science 2008)

Herpes virus movement in axon

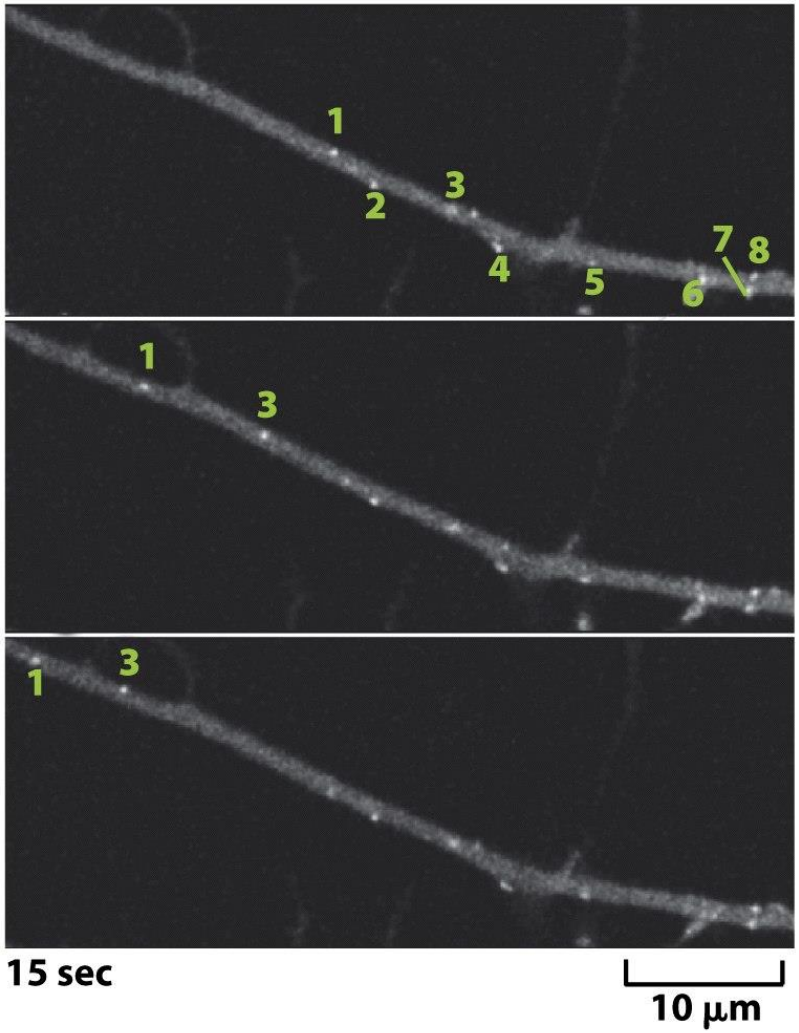


Figure 24-39 *Molecular Biology of the Cell* (© Garland Science 2008)

Error prone replication dominates evolution

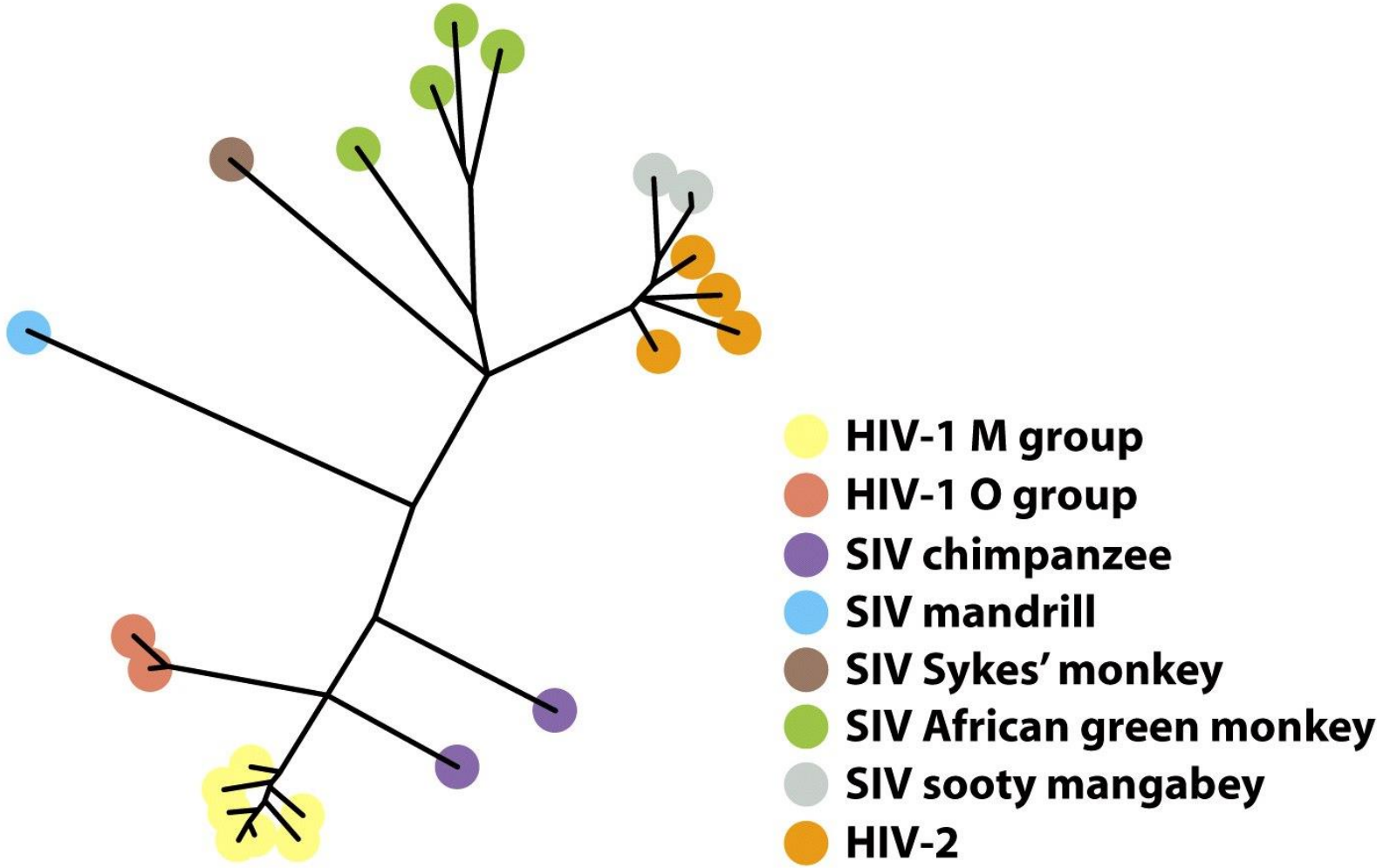
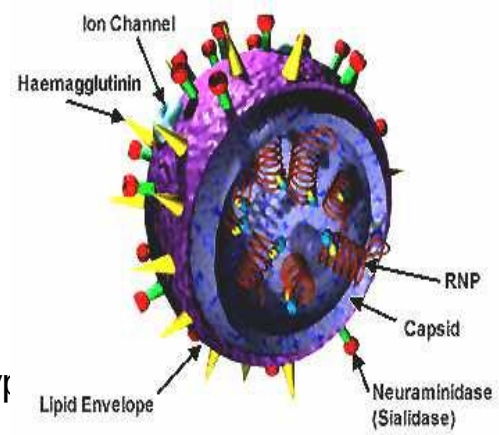


Figure 24-42 *Molecular Biology of the Cell* (© Garland Science 2008)

How Do Viruses enter animal cells

- **Influenza A, B, C's: Three types of influenza viruses.**
  - Human influenza A and B viruses cause seasonal epidemics in winter.
  - Influenza C infections cause only a mild respiratory illness.



- **H (what) N (who)? Influenza A subtypes**

  Based on two viral surface proteins:
  - hemagglutinin **(H)**
  - neuraminidase **(N).**
  - 16 different hemagglutinin subtypes and 9 different neuraminidase subtyp
  - Current subtypes of influenza A viruses found in people: H1N1 & H3N2.
  - Spring 2009, a new influenza A (H1N1) virus emerged, very different from regular human influenza A (H1N1) and caused a pandemic.

- **Influenza B viruses are not divided into subtypes.**
- **Regular influenza A (H1N1), A (H3N2), and influenza B viruses are included in each year's seasonal influenza vaccine.**
- **The seasonal flu vaccine does not protect against influenza C viruses.**
- **This year's seasonal vaccine will not protect against the 2009 H1N1 virus.**

Influenza is caused by an **enveloped ssRNA** virus.

Image: Influenza A Virus, National Institutes of Health; Information: Influenza Types, CDC

Viral disease

An **influenza pandemic** is an epidemic of an influenza virus that spreads on a worldwide scale infecting many people.

In contrast to regular seasonal epidemics of influenza, pandemics occur irregularly, with the 1918 Spanish flu the most serious pandemic in recent history.

Pandemics can cause high levels of mortality, with the Spanish influenza having been responsible for the deaths of 50 – 100 million people worldwide.

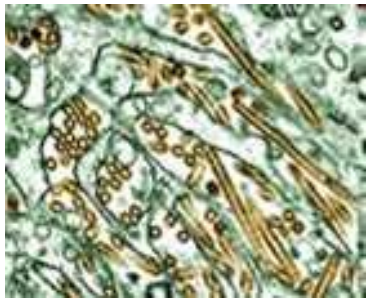
~ 3 influenza pandemics in each century for the last 300 years.

Most recent ones:

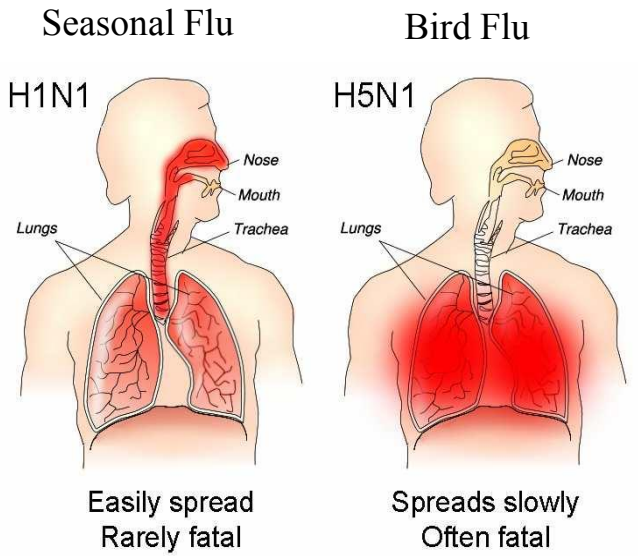
- Asian Flu in 1957
- Hong Kong Flu in 1968
- Swine Flu in 2009 - 2010

Occur when a new strain of influenza virus is transmitted to humans from animals (especially pigs, chickens and ducks).

These new strains are unaffected by immunity people may have to older human flu strains, so can spread rapidly.



Avian influenza A H5N1 viruses (seen in gold) do not usually infect humans; however, several instances of human infections and outbreaks have been reported since 1997 (Source CDC PHIL #1841).



For more info see: http://www.pandemicflu.gov

Viral pandemics

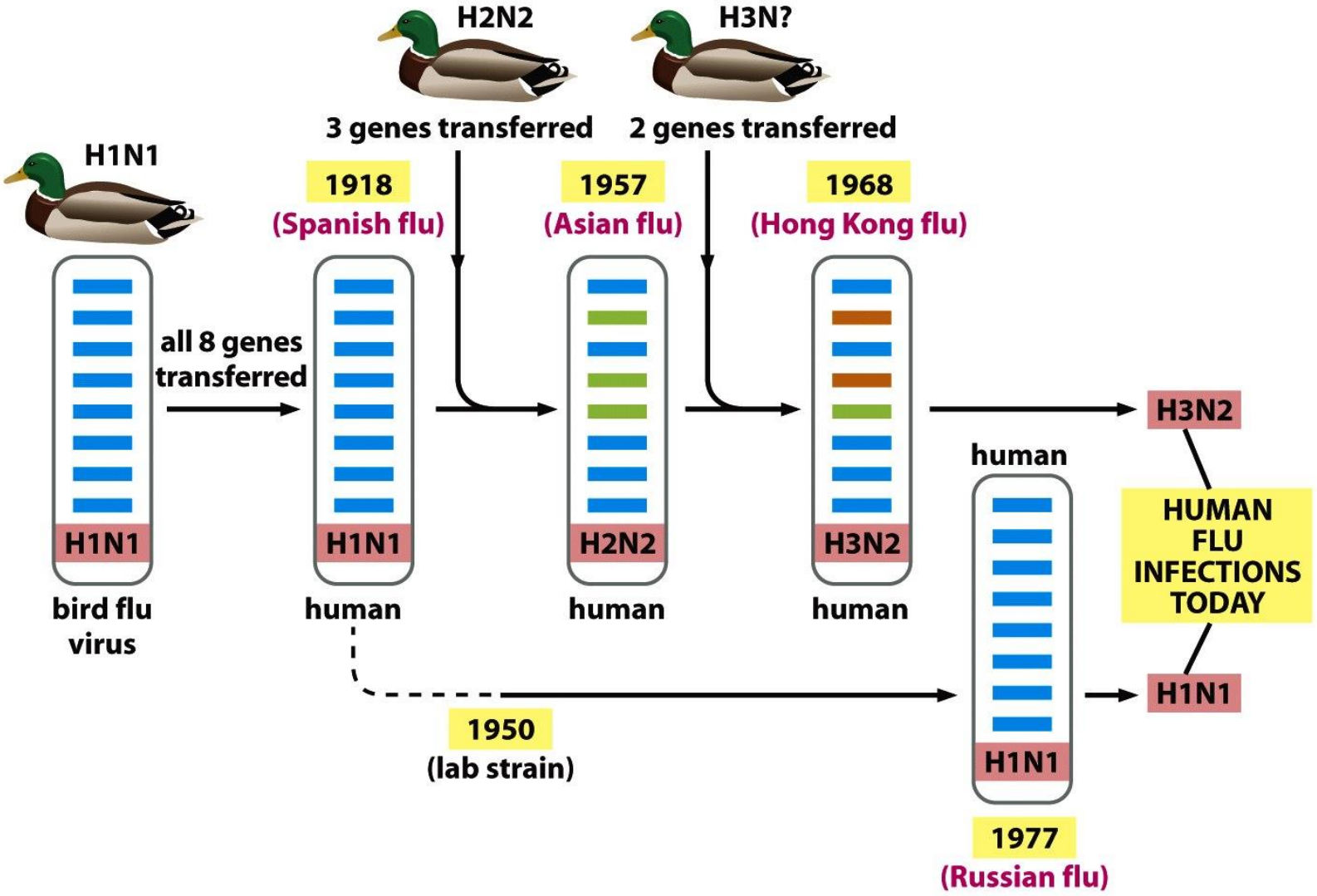
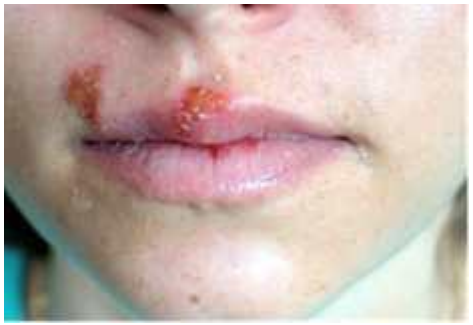


Figure 24-43 *Molecular Biology of the Cell* (© Garland Science 2008)

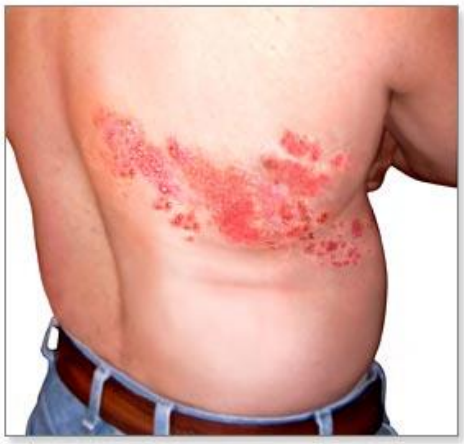
Herpes virus

HERPESVIRIDAE: Large family of enveloped dsDNA viruses that cause diseases in animals, including humans.

- **Family name derived from the Greek word herpein ("to creep"), referring to the latent, recurring infections typical of this group of viruses. Seven known herpes viruses infect humans.**

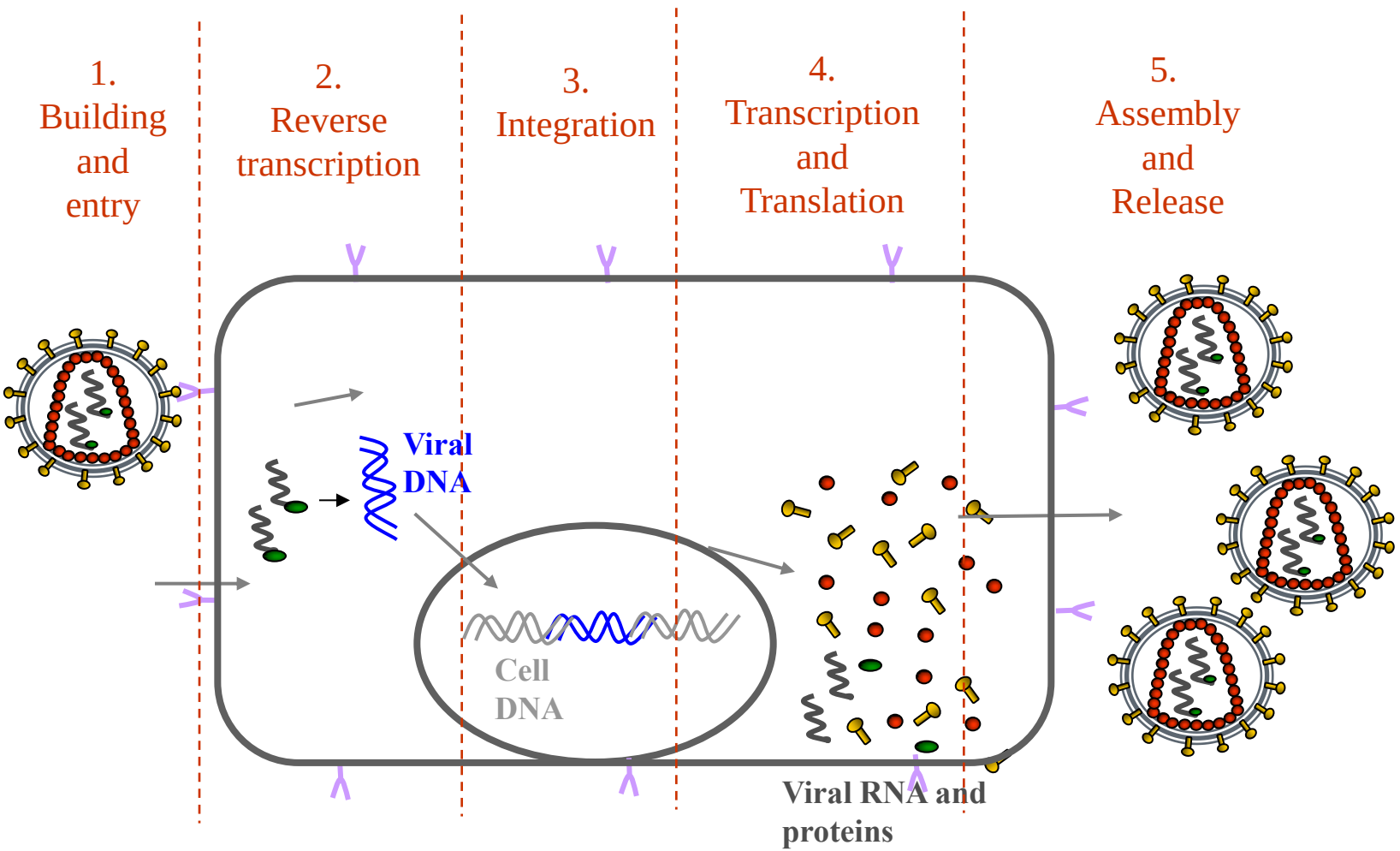


- **Enveloped DNA viruses of the Herpesviridae that often cause blistery lesions in the skin and mucous membranes**
- **Antiviral treatments treat active infection but often do not cure latent viral disease.**
- **Herpesviruses exist in latent and actively replicating forms. The following are herpesviruses:**
  - **Cytomegalovirus** can be silent or cause brain damage in newborns and blindness in AIDS patients
  - **Epstein-Barr virus** can cause infectious mononucleosis and is associated with Burkitt's lymphoma
  - **Varicella zoster** causes chicken pox and shingles
  - **Herpes simplex 2** (HSV2) causes genital lesions
  - **HSV1** is associated with mouth chancre sores.



Shingles

Retrovirus



The Reproductive Cycle of a Retrovirus

A retrovirus is an **enveloped** **ssRNA** virus. It relies on the enzyme ***reverse transcriptase*** to use its RNA genome to build DNA, which can then be integrated into the host's genome. The virus then replicates as part of the cell's DNA.

How Can Viral Diseases Be Prevented and Treated?

Good hygiene

- Avoid contact with contaminated food, water, fecal material or body fluids.
- Wash hands frequently.

Vaccines

- Stimulate natural defenses with in the body.
- Contain a component of or a weakened or ‘killed” virus particles.
- Are developed for many once common illnesses such as smallpox, polio, mumps, chicken pox.
- Not available for all viruses.

Anti-viral drugs (but not antibiotics)

- Available for only a few viruses.
- Inhibit some virus development and/or relieve symptoms.

Image: Purchased from iStock,#5255912.jpg, small.

Modified “Live” Virus Vaccines vs “Killed” Viruses Vaccines

Modified live virus vaccines contain viruses that have been altered (attenuated) to virulence, yet retain their antigenic properties and induce a immune response.

MLV vaccines must replicate after inoculation to produce enough antigen to produce an immune response.

***Advantages*:**

- One dose
- Quicker immune response
- Stronger, more durable response
- Fewer post-vaccine reactions

***Disadvantages* :**

- Possible reversion to virulence
- Possible viral shedding
-Not recommended for pregnant animals or animals in contact with pregnant animals
- Improper handling may inactivate *(example: must be used quickly following rehydration)*

Killed virus vaccines contain viruses that have been treated by chemical or physical means to prevent them from replicating in the vaccinate.

***Advantages*:**

- Safer
- No possibility for reversion
- Recommended for pregnant animals
- Stable in storage

***Disadvantages* :**

- Multiple doses required
- Weaker immune response
- Shorter duration immune response

- Hypersensitivity reactions more common

Eradication of polio

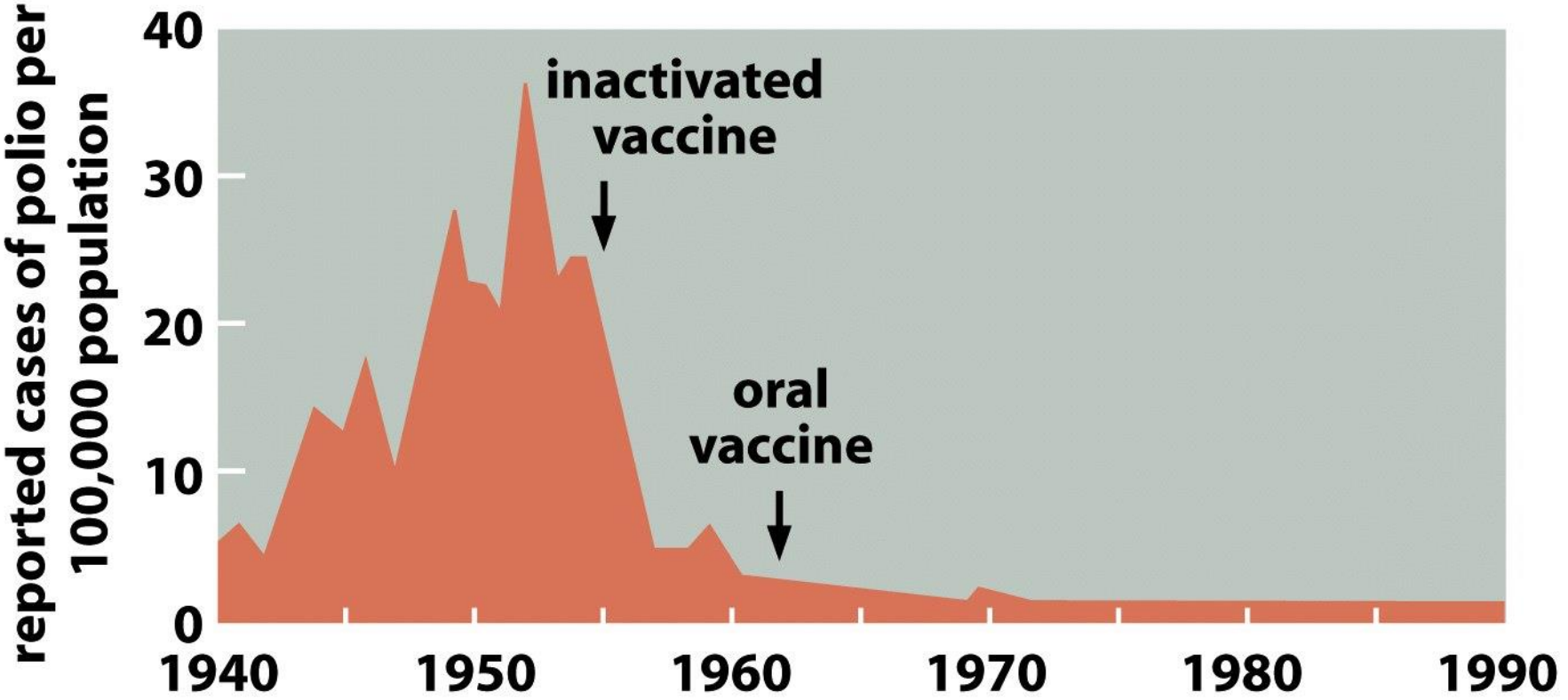


Figure 24-17 *Molecular Biology of the Cell* (© Garland Science 2008)

Pathogen types: eukaryotes

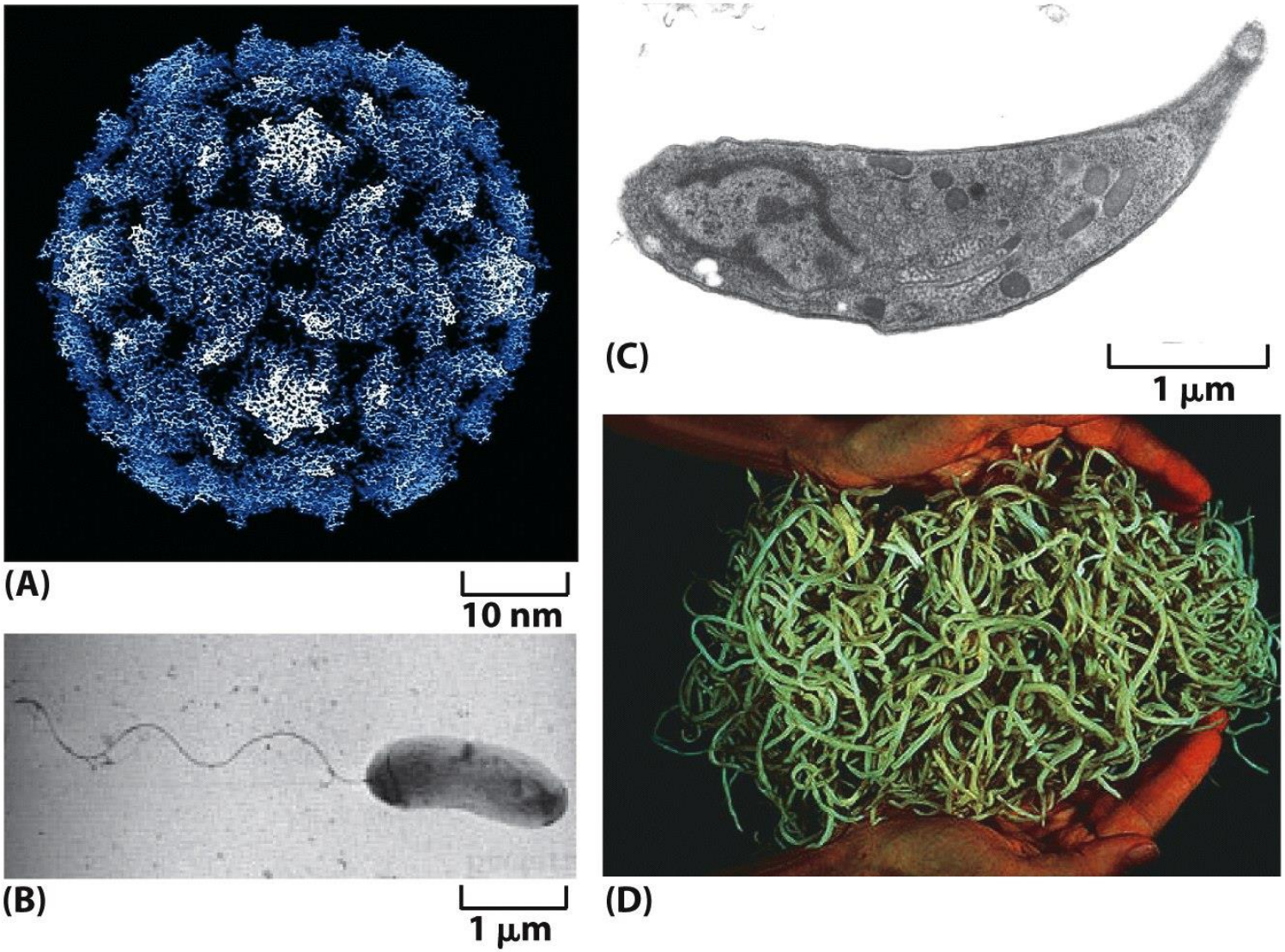


Figure 24-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Pathogenic Fungi

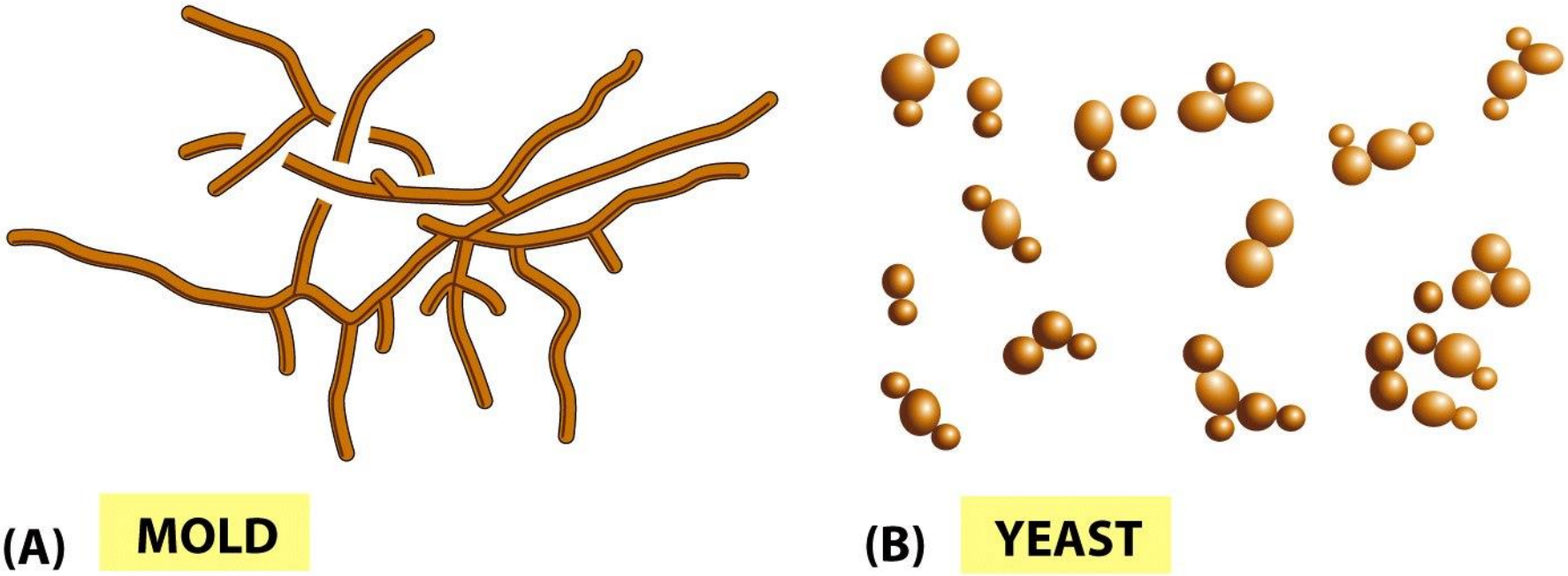


Figure 24-9 *Molecular Biology of the Cell* (© Garland Science 2008)

Protozoal parasites (malaria)

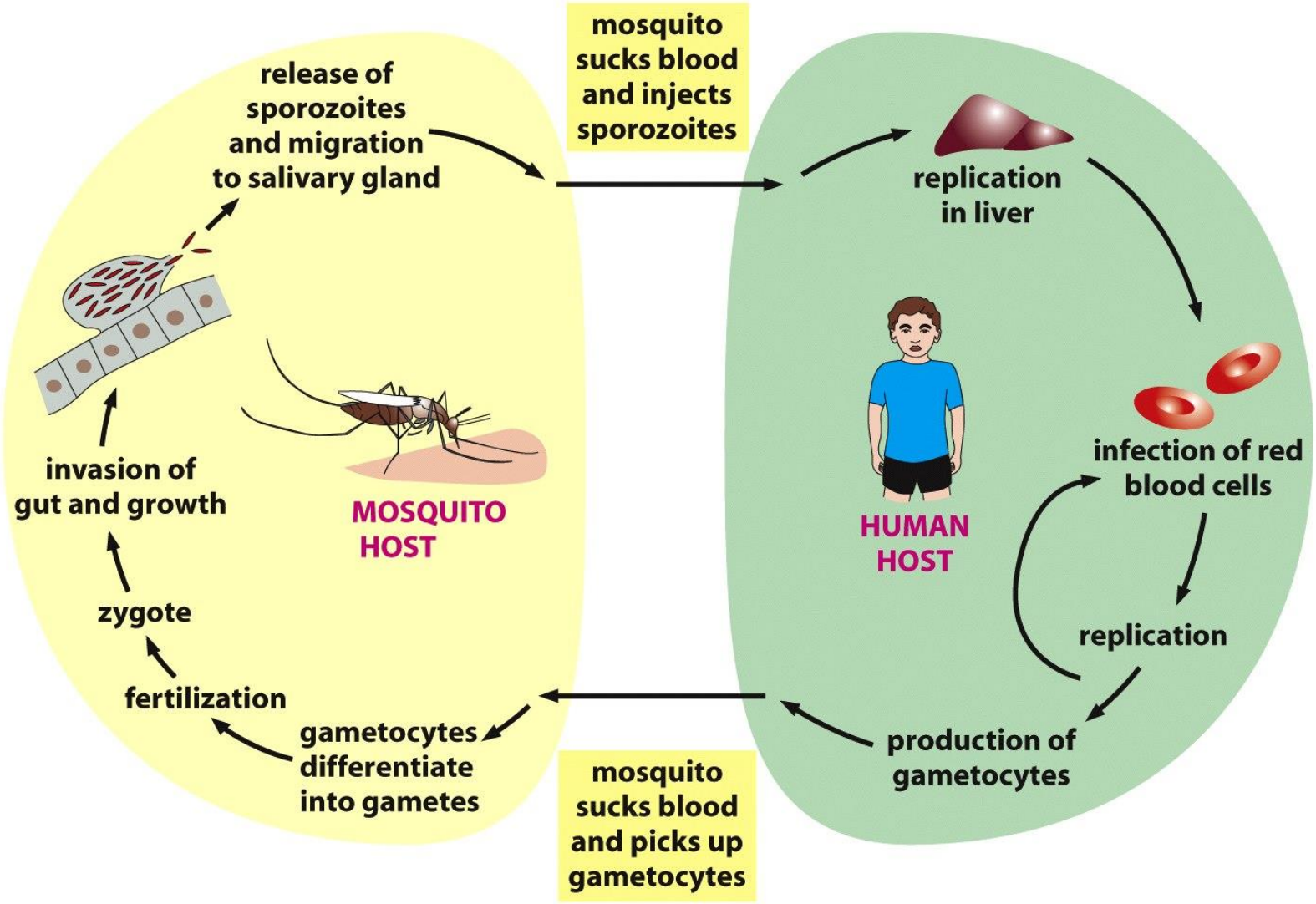


Figure 24-10a *Molecular Biology of the Cell* (© Garland Science 2008)

Protozoal parasites (malaria)

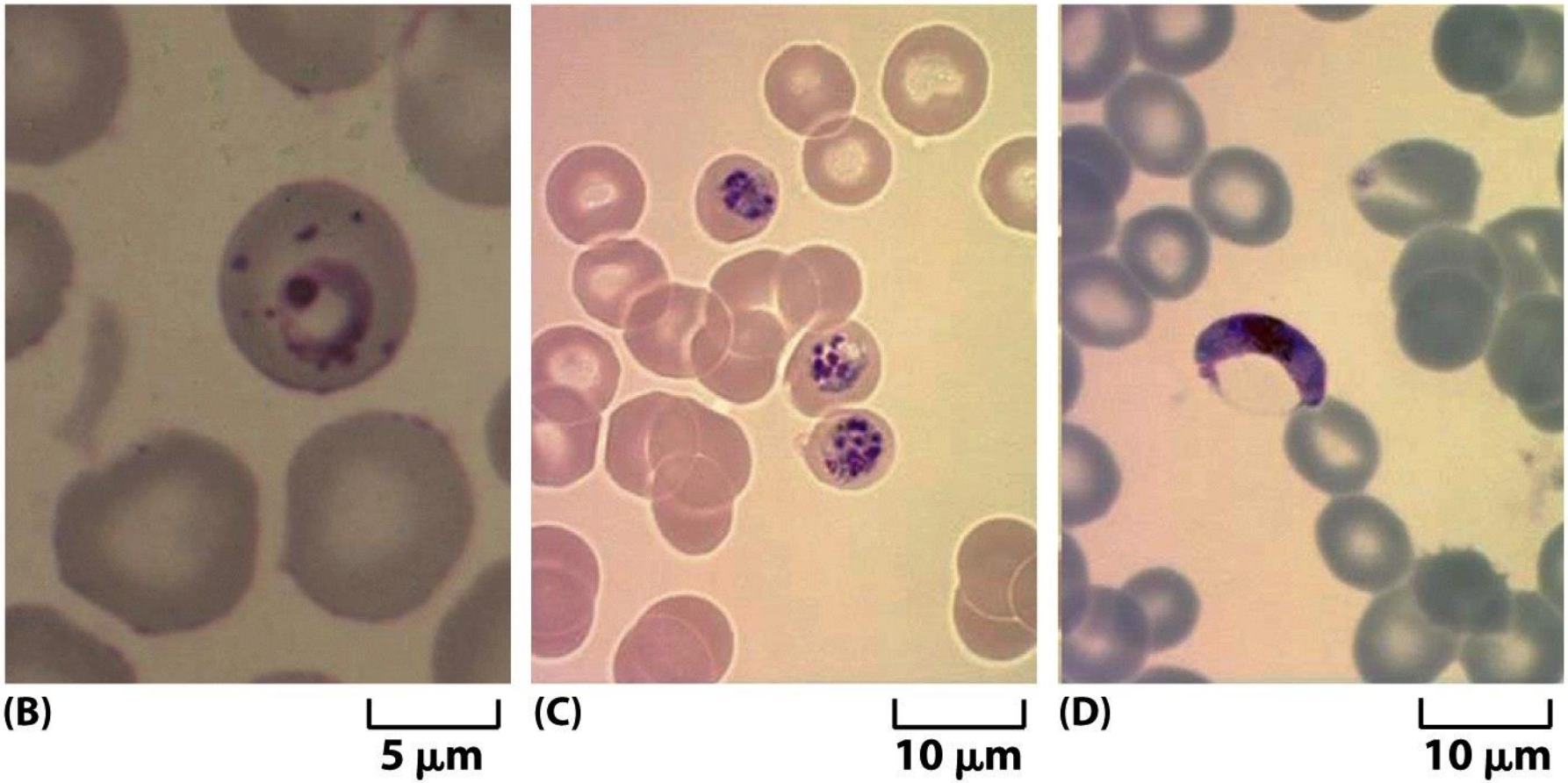


Figure 24-10b-d *Molecular Biology of the Cell* (© Garland Science 2008)

Toxoplasma gondii lifecycle

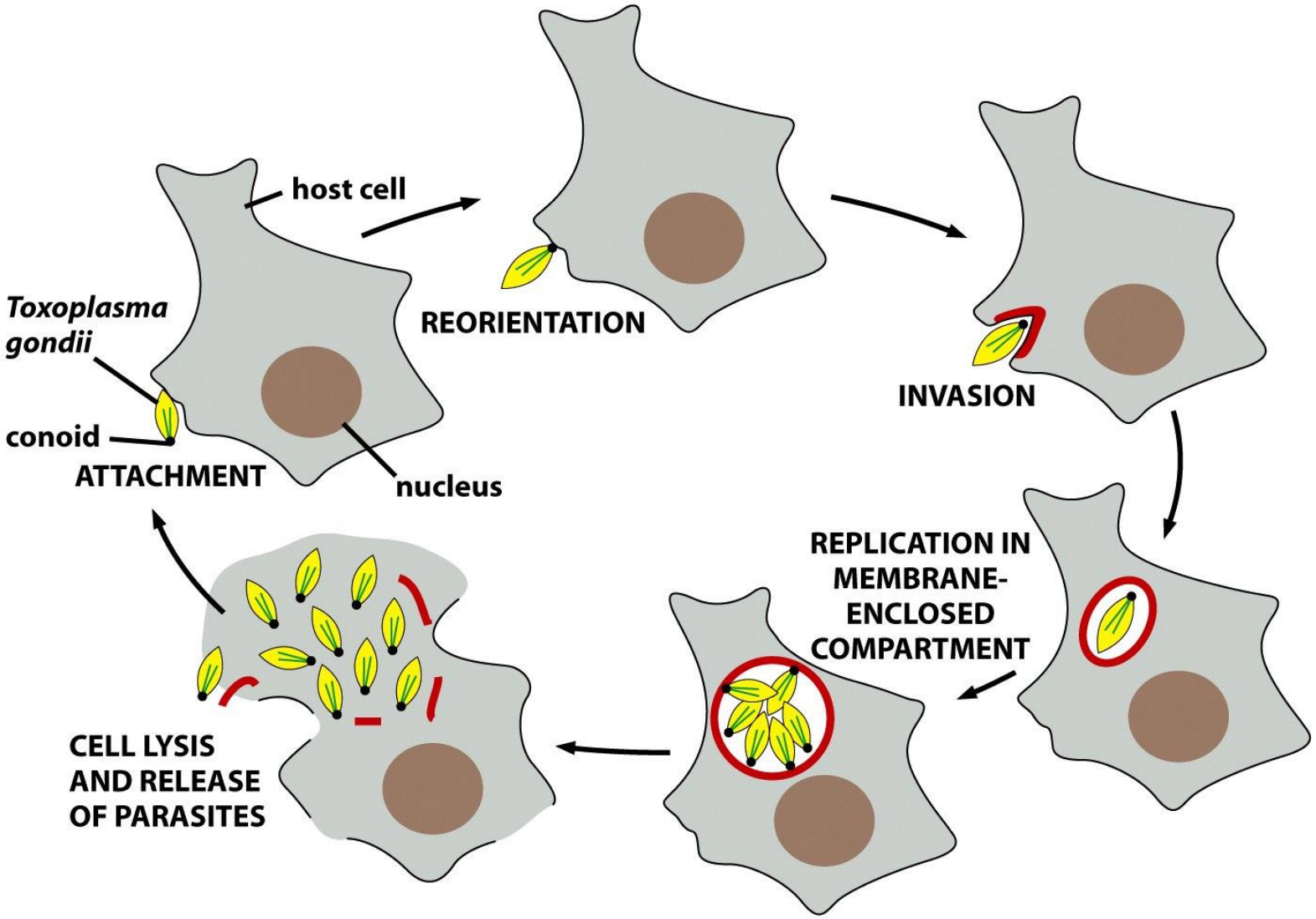


Figure 24-27a *Molecular Biology of the Cell* (© Garland Science 2008)

Toxoplasma gondii lifecycle

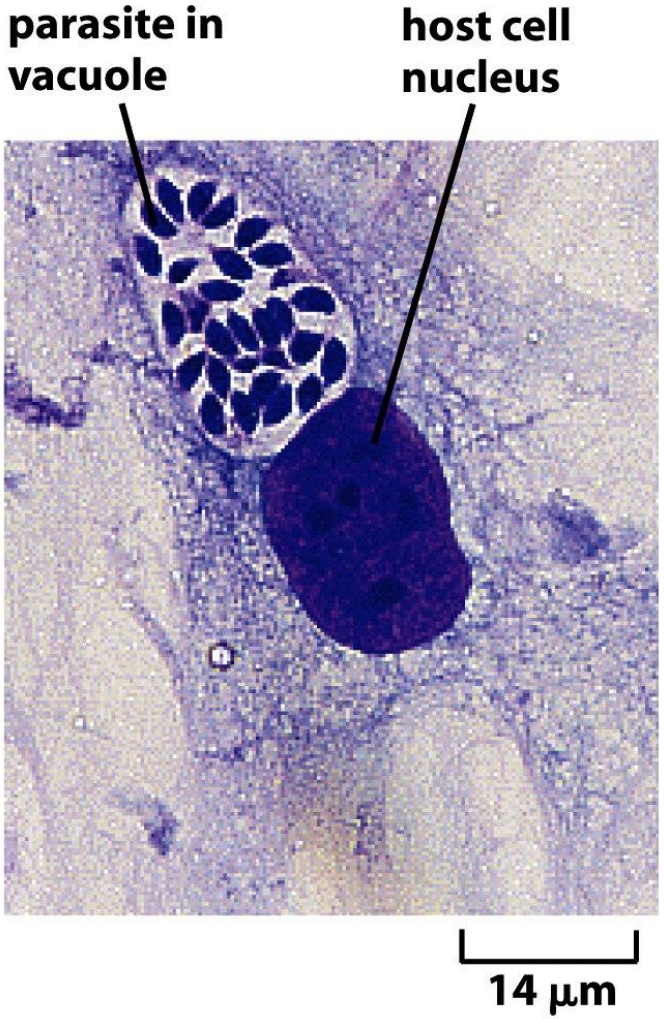


Figure 24-27b *Molecular Biology of the Cell* (© Garland Science 2008)

Pathogen types: prions

?

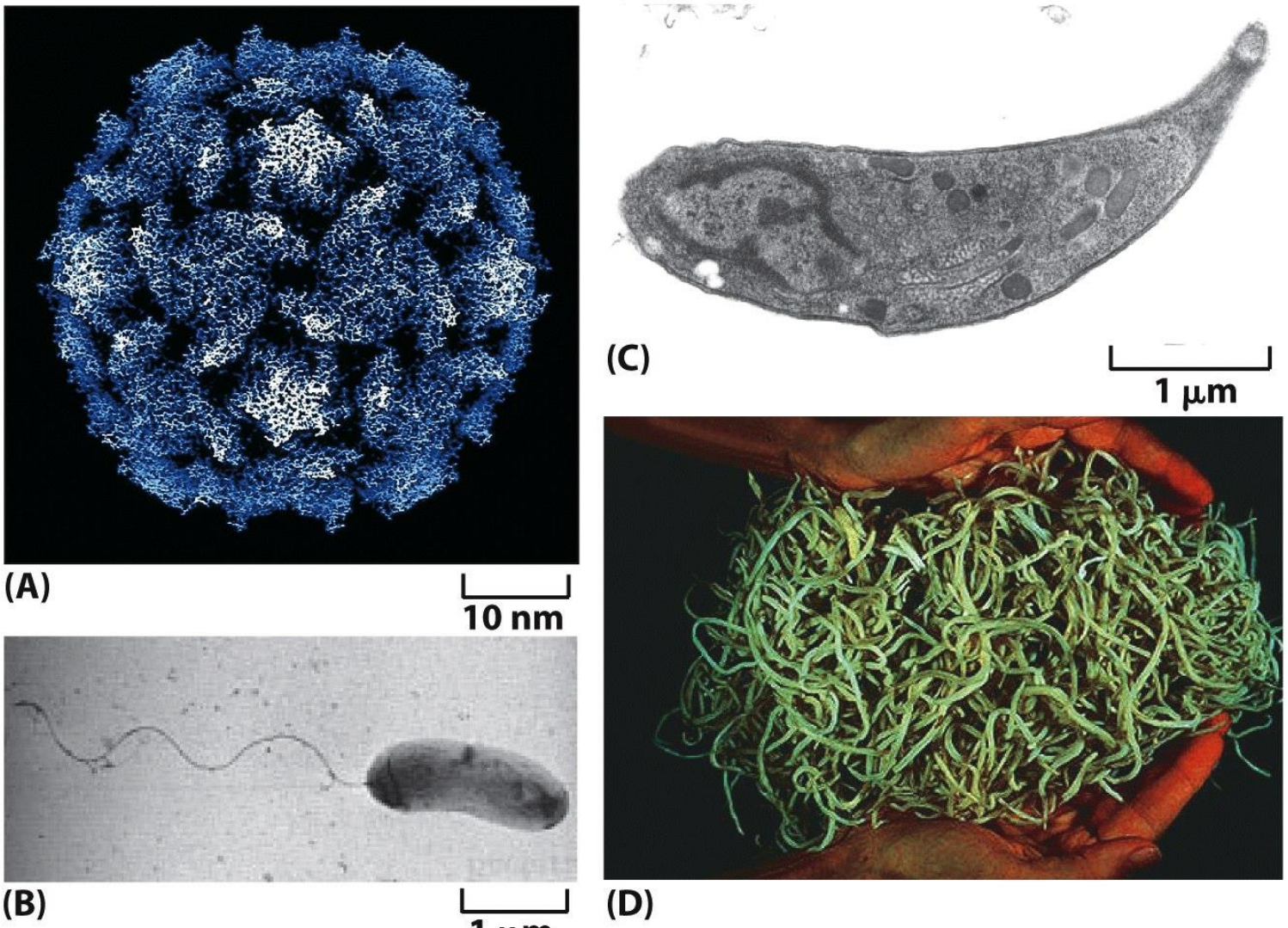
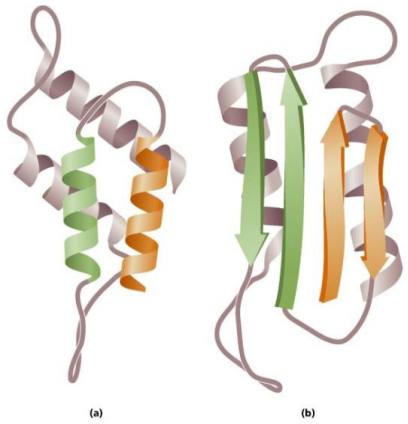


Figure 24-3 *Molecular Biology of the Cell* (© Garland Science 2008)

Prions



Prions: infectious agents even simpler than viruses.

They are made of protein but have *no nucleic acid*.

Responsible for fatal neurodegenerative diseases called *transmissible spongiform encephalopathies (TSEs).*

Good Protein Gone Bad?

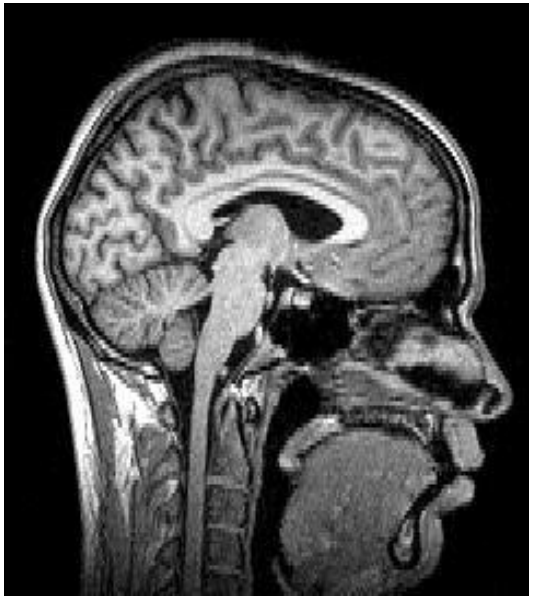
Abnormal form of a normally harmless protein found in mammals and birds.

Can enter brain through infection, after being *ingested*, or arise from a *mutation*.

In brain, causes normal proteins to refold into abnormal shape.

As prion proteins multiply, neurons are destroyed and brain tissue becomes riddled with holes.

Unlike all other known agents of infection, they lack nucleic acid



TSEs include:

- Creutzfeldt-Jakob disease
- mad cow disease
- scrapie (neuro disease of sheep & goats)

can only be destroyed through incineration.

Prion caused neural degeneration

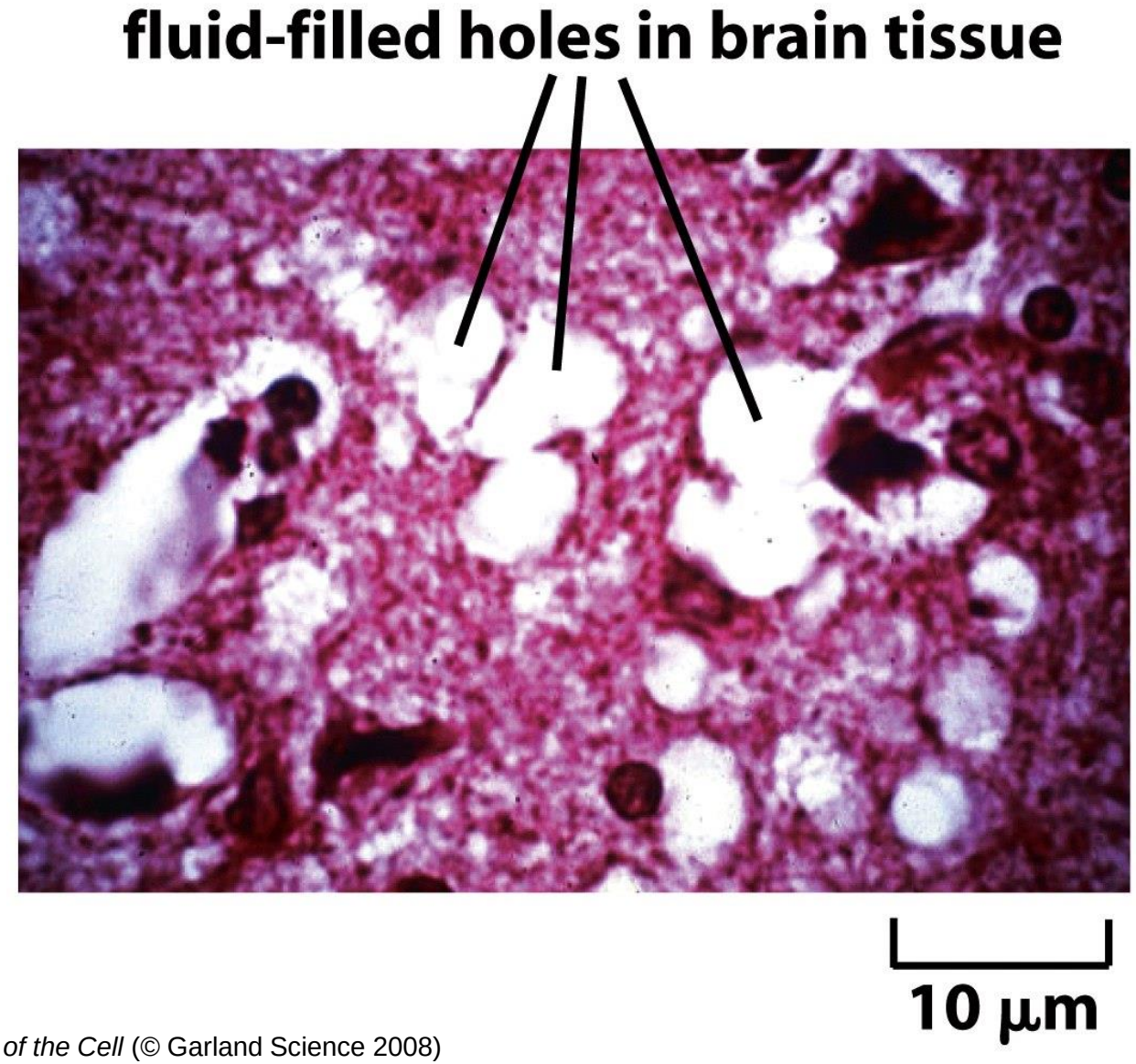
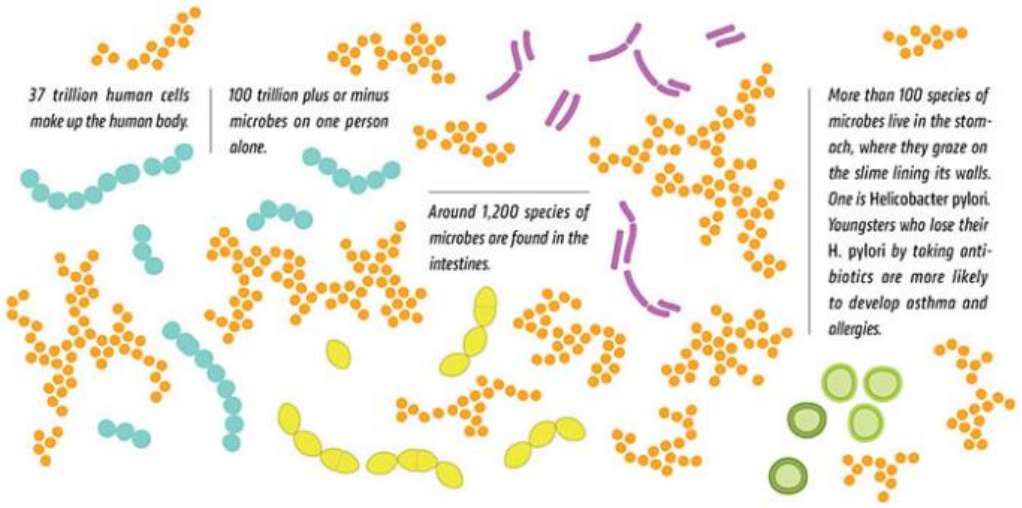
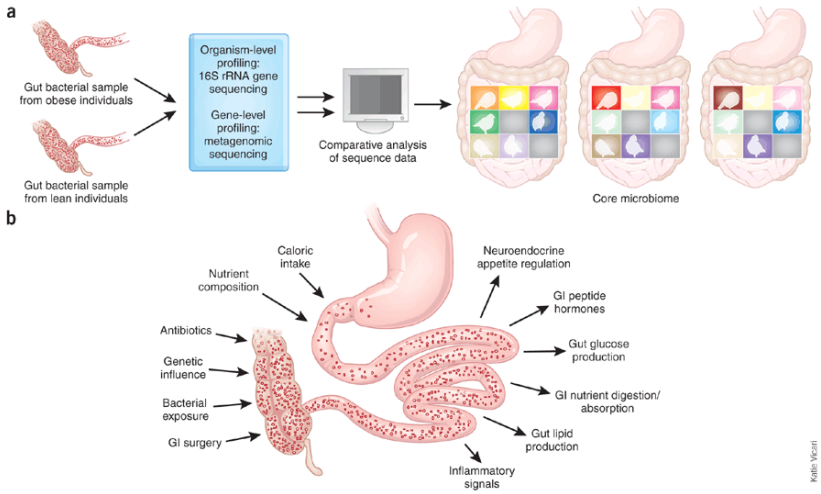


Figure 24-18 *Molecular Biology of the Cell* (© Garland Science 2008)

The Microbiome





3 key functions:

1. Digesting fibre
2. Protection against pathogens
3. Immune response