STEM CELLS AND THERAPEUTIC CLONING

Gene expression

- The overall process by which genetic information flows from genes to proteins—that is, from genotype to phenotype—is **gene expression**.
- Prokaryotes and eukaryotes precisely regulate gene expression in response to environmental conditions
- In multicellular eukaryotes, gene expression regulates development and is responsible for differences in cell types

Concept 18.4: A program of differential gene expression leads to the different cell types in a multicellular organism

- During embryonic development, a fertilized egg gives rise to many different cell types
- Cells are organized successively into tissues, organs, organ systems, and the whole organism
- Cell **differentiation** is the process by which cells become specialized in structure and function
- Materials in the egg set up a program of gene regulation that is carried out as cells divide

Development

- As a zygote develops into a multicellular organism, individual cells must undergo **differentiation**, becoming specialized in structure and function.
  - Each cell type must maintain a specific regimen of gene expression in which some genes are expressed and others are not.
  - The differences between cell types, therefore, are not due to different genes being present but instead due to selective gene expression.

Differential Gene Expression

- Almost all the cells in an organism contain an identical genome
- Differences between cell types result from **differential gene expression**, the expression of different genes by cells with the same genome
- Abnormalities in gene expression can lead to diseases including cancer

Development: from unspecialized to specialized

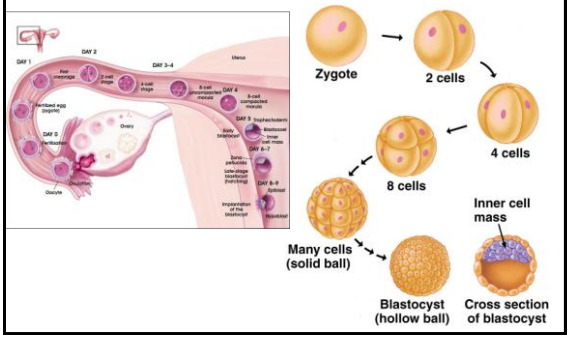


Figure 27.10

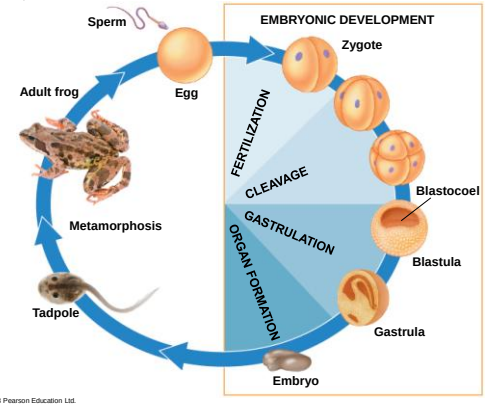
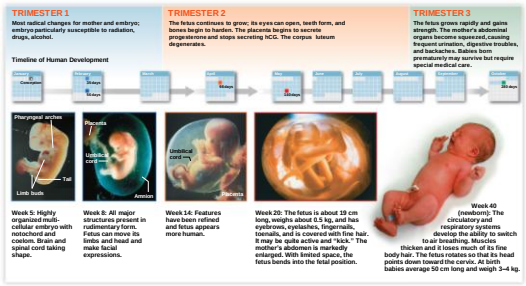
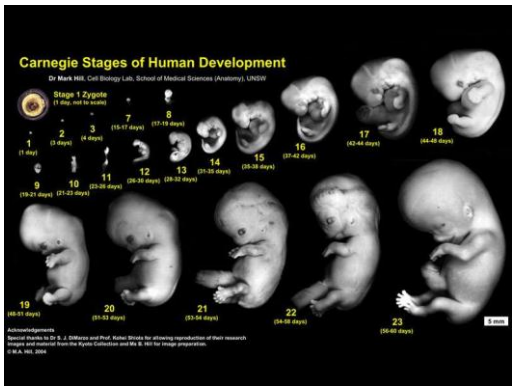


Figure 27.16

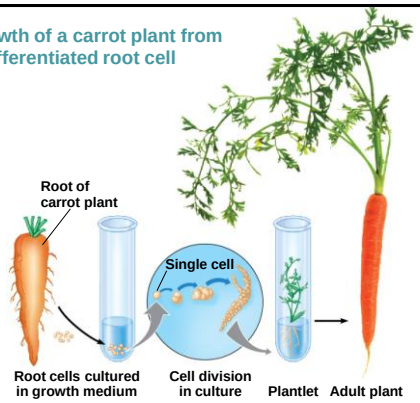




Plant cloning shows that differentiated cells may retain all of their genetic potential

- A **clone** is an individual organism created by asexual reproduction and thus genetically identical to a single parent.
- Any cell capable of producing every kind of specialized cell in an organism is said to be **totipotent**.
- **Regeneration**, the regrowth of lost body parts, demonstrates that differentiation need not impair an animal cell's genetic potential.

Growth of a carrot plant from a differentiated root cell



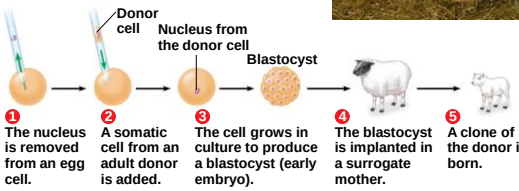
Cloning of animals

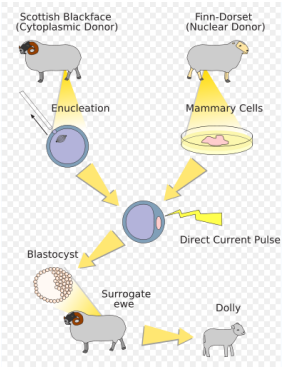
- The first mammal to be cloned was an adult ewe (female sheep) in 1996.
- However, the outcomes of animal cloning have not lived up to initial expectations.
  - Cloned animals are often abnormal, with shortened life spans and increased incidences of age-related diseases.
  - The difficulties in producing a healthy clone highlight the complex role genes play in the growth of an organism.

Biologists can clone animals via nuclear transplantation

- In the process of animal cloning called **nuclear transplantation**, DNA from a donor cell is inserted into a nucleus-free host egg, resulting in a clone of the DNA donor.
- If the animal being cloned is a mammal, the blastocyst is then implanted into the uterus of a surrogate mother. This type of cloning is called **reproductive cloning** because it can result in the birth of a new living individual.

Dolly the Sheep
July 5, 1996 – February 14, 2003





Biologists can clone animals via nuclear transplantation

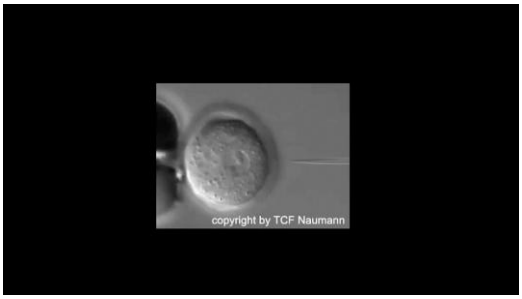
- Dolly's premature death in 2003, as well as that of another cloned sheep from another experiment, led to speculation that her cells were not as healthy as those of a normal sheep
- This possibly reflects incomplete reprogramming of the original transplanted nucleus

Biologists can clone animals via nuclear transplantation

Checkpoint question Why does the history of cloning sheep suggest human cloning should not be pursued?

- Dolly was the only lamb that survived to adulthood from 277 attempts. Such experimentation with humans raises ethical questions.

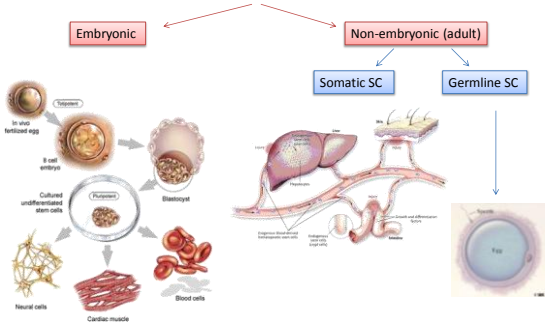
Video: Pronuclear Injection



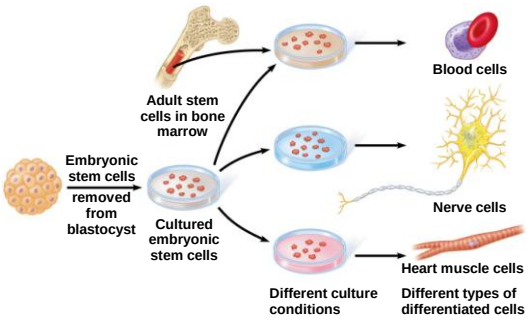
Therapeutic cloning can produce stem cells with great medical potential

- The goal of **therapeutic cloning** is to produce **embryonic stem cells**.
  - Such cells may eventually be used for a variety of therapeutic purposes.
  - Like embryonic stem cells, **adult stem cells** can both perpetuate themselves in culture and give rise to differentiated cells.
  - Unlike embryonic stem cells, adult stem cells normally give rise to only a limited range of cell types.

Stem Cells



Therapeutic cloning using stem cells

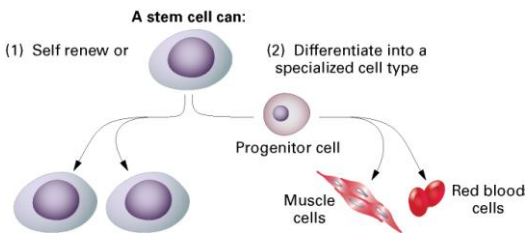


Stem cell therapy may one day cure diseases.

macular degeneration

may one day be cured with injections of retinal cells derived from stem cells

A stem cell has two basic characteristics.

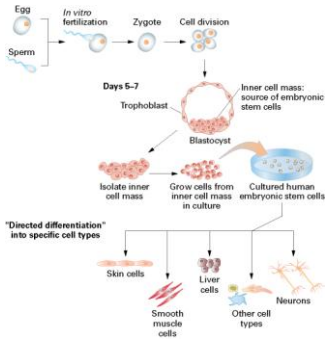


Stem cells are relatively unspecialized cells that can both reproduce indefinitely and, under certain conditions, differentiate into one or more specialized cell types

Embryonic and Adult Stem Cells

- Many early embryos contain stem cells capable of giving rise to differentiated embryonic cells of any type
- In culture, these embryonic stem (ES) cells reproduce indefinitely, and depending on culture conditions, can be made to differentiate into a variety of specialized cells
- Adult stem cells can generate multiple (but not all) cell types and are used in the body to replace nonreproducing cells as needed

ESC differentiation



Adults have stem cells too

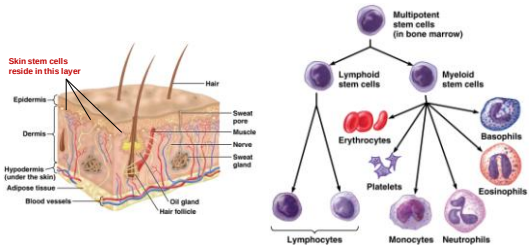
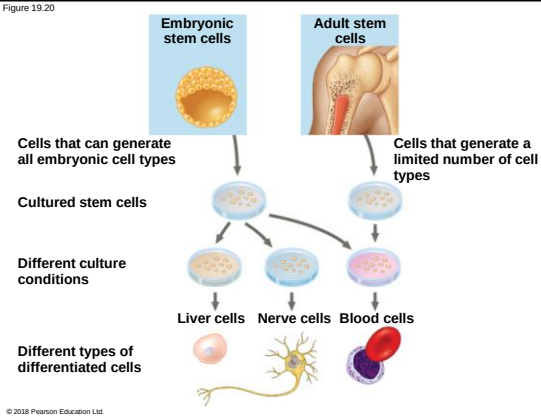


Figure 19.20



- How are humans being treated with stem cells?

Regenerative medicine: Stem cell–derived cells, tissues, or organs might be transplanted, or stem cells inside tissues may be stimulated to replace a failing body part.

- The main aim of cloning ES cells is to produce cells for treating disease
- The process is thus called therapeutic cloning
- Opinions vary about the morality of therapeutic cloning

Embryonic stem cells: safe or tumor producing?

Embryonic stem cells

↓ differentiated into

Dopamine-producing neurons

↓ injected into brains of rats with Parkinson's disease

Symptoms were reduced, but brain tumors formed.

Embryonic stem cell trial therapies

To treat spinal cord injury:

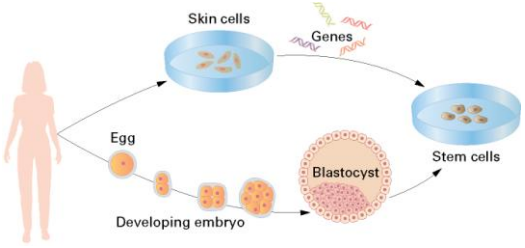
To treat macular degeneration:

A view with normal vision

A view with macular degeneration

Induced pluripotent stem cells: No therapies yet

Reprogramming cells (reversing differentiation)



Making pluripotent cells from embryos

Somatic (adult) stem cells: numerous therapies

Blood stem cells

Some cancers can be cured with blood stem cells.

- How can stem cell therapy be personalized?

Comparing two methods for making personalized (immune system-matched) pluripotent stem cells

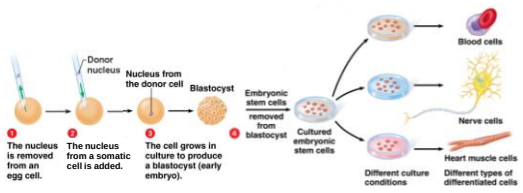
Using embryonic stem cells

- Technically more challenging
- Begins with a human egg cell
- An embryo is created and destroyed to produce the personalized cells (ethical issues).

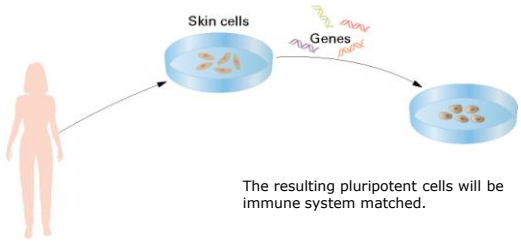
Using iPS cells

- Technically easier to produce
- Begins with a somatic cell
- An embryo is not created during the process.

Making personalized ES cells (“therapeutic cloning”)



Personalized iPS cells

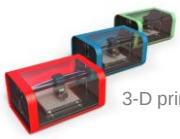


The resulting pluripotent cells will be immune system matched.

- What might the future hold for stem cells?

Making organs in the lab

Biodegradable scaffolds

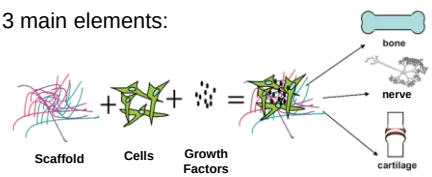


3-D printing

Decellularized scaffolds from cadavers

Tissue Engineering

- Applies principles of engineering and life sciences for the development of biological substitutes that restore, maintain or improve tissue function.
- 3 main elements:



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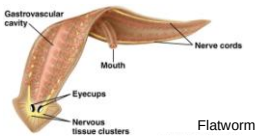
The World's First Synthetic Trachea Made of Nanocomposite 3D Scaffold and Autologous Stem Cells, Implanted in a 36-year-old Patient in June 2011

Trends in Biotechnology 2016 34, 1010-1021DOI: (10.1016/j.tibtech.2016.05.012)

In 1997 Dr Jay Vacanti grew a human ear from cartilage cells the back of a mouse

Spinach Leaf Transformed Into Beating Human Heart Tissue

Regeneration



Flatworm

SOURCES FOR MORE INFORMATION

- **Overview videos about embryonic stem cells:**

http://vimeo.com/75258017?from=outro-embed
http://www.hhmi.org/biointeractive/creating-embryonic-stem-cell-lines
http://www.dnalc.org/view/16991-How-Embryonic-Stem-Cell-Lines-are-Made.html

- **Articles about first embryonic stem cell clinical trials:**

http://investor.biotimeinc.com/phoenix.zhtml?c=83805&p=irol-newsArticle_print&ID=1933710&highlight=

- **Article about first embryonic stem cell clinical trials to treat macular degeneration:**

http://www.technologyreview.com/news/526591/stem-cell-treatment-for-blindness-moving-through-patient-testing/

SOURCES FOR MORE INFORMATION

- **United Network for Organ Sharing (UNOS) website with current data about organ transplants:**

http://www.unos.org/donation/index.php?topic=data

- **Reference for embryonic stem cell treatment of Parkinson-like rats:**

http://onlinelibrary.wiley.com/doi/10.1634/stemcells.21-2-171/pdf

- **Video explaining macular degeneration:**

http://www.youtube.com/watch?v=WVDxN161Maw

- **Overview video about induced pluripotent stem (iPS) cells:**

http://stemcellthailand.org/induced-pluripotent-stem-cells-ips-ipscs-hipscs/

SOURCES FOR MORE INFORMATION

- **Explore niches in the human body for somatic stem cells:**

http://learn.genetics.utah.edu/content/stemcells/sctypes/

- **Article and video about building a heart:**

http://www.nature.com/news/tissue-engineering-how-to-build-a-heart-1.13327

- **TED Talk video by Dr. Anthony Atala about 3-D printing organs:**

https://www.ted.com/talks/anthony_atala_printing_a_human_kidney

SOURCES FOR MORE INFORMATION

- **HHMI videos on regeneration:**

http://www.hhmi.org/biointeractive/newt-limb-regeneration
http://www.hhmi.org/biointeractive/zebrafish-heart-regeneration
A discussion with a scientist Alejandro Sanchez-Alvarado:
http://www.hhmi.org/biointeractive/planarian-regeneration-and-stem-cells

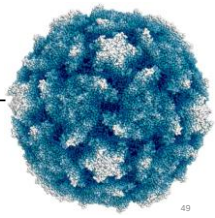
- **Good general overview sites about stem cells:**

http://stemcells.nih.gov
http://www.eurostemcell.org/

THE GENETICS OF VIRUSES AND BACTERIA

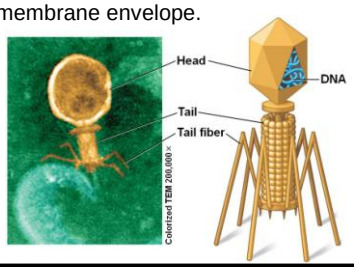
Introduction

- Polio is caused by a highly contagious virus.
- Until a 2013 outbreak occurred in Syria, polio was thought to have been all but eradicated in the country.
- Combating any virus requires a detailed understanding of nucleic acid—DNA and RNA—and how it serves as the molecule of heredity.



10.17 Viral DNA may become part of the host chromosome

- A **virus** is an infectious particle consisting of little more than "genes in a box": a bit of nucleic acid wrapped in a protein coat called a **capsid** and, in some cases, a membrane envelope.



10.17 Viral DNA may become part of the host chromosome

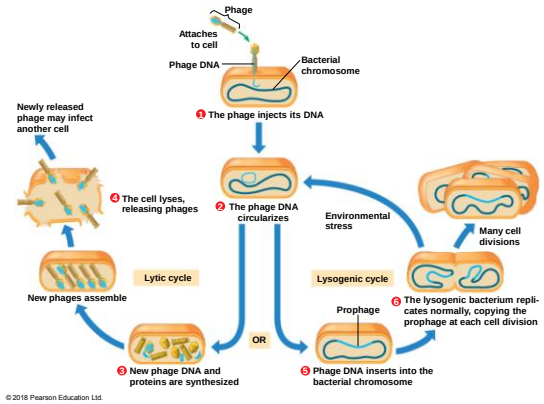
- When phage DNA enters a **lytic cycle** inside a bacterium, it is replicated, transcribed, and translated.
- The new viral DNA and protein molecules then assemble into new phages, which burst from the host cell.

10.17 Viral DNA may become part of the host chromosome

- In the **lysogenic cycle**, phage DNA inserts into the host chromosome and is passed on to generations of daughter cells.
  - Once inserted, the phage DNA is referred to as a **prophage**, and most of its genes are inactive.
  - Later, it may initiate phage production.

Checkpoint question Describe one way a virus can perpetuate its genes without destroying its host cell. What is this type of replication cycle called?

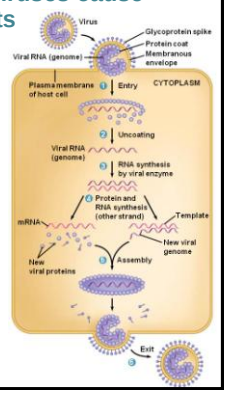
Figure 10.17



10.18 CONNECTION: Many viruses cause disease in animals and plants

- Flu viruses and most plant viruses have RNA, rather than DNA, as their genetic material.
- Some animal viruses steal a bit of host cell membrane as a protective envelope.

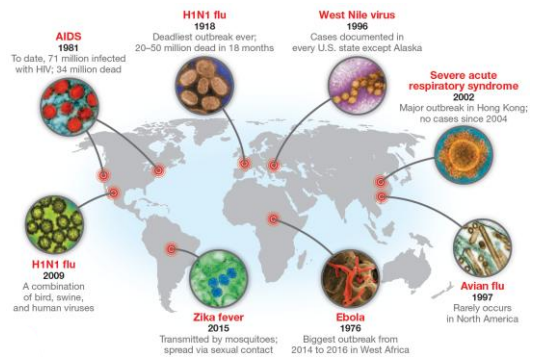
Checkpoint question
Explain how some viruses replicate without having DNA.



10.19 EVOLUTION CONNECTION: Emerging viruses threaten human health

- **Emerging viruses** are ones that seem to burst on to the scene, becoming apparent to the medical community quite suddenly.
- One familiar example is **HIV** (human immunodeficiency virus), the virus that causes **AIDS** (acquired immunodeficiency syndrome).

Checkpoint question Why doesn't a flu shot one year give us immunity to flu in subsequent years?

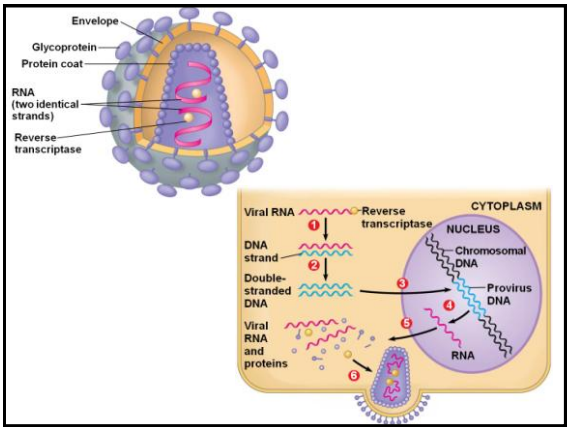


A map of major emerging virus outbreaks of the past 100 years

10.20 The AIDS virus makes DNA on an RNA template

- HIV is a **retrovirus**: It uses RNA as a template for making DNA, which then inserts into a host chromosome.
- These viruses carry molecules of an enzyme called **reverse transcriptase**, which catalyzes reverse transcription: the synthesis of DNA on an RNA template.

Checkpoint question Why is HIV reverse transcriptase a good target for anti-AIDS drug therapy?



10.21 Prions are infectious proteins

- **Prions** are infectious proteins that can cause brain diseases in animals.
- When the prion gets into a cell containing the normal form of the protein, the prion somehow converts normal protein molecules to misfolded versions.

Checkpoint question What makes prions different from all other known infectious agents?

10.22 Bacteria can transfer DNA in three ways

- Bacteria use three mechanisms to move genes from cell to cell.
  1. **Transformation** is the uptake of DNA from the surrounding environment.
  2. **Transduction** is gene transfer by phages.
  3. **Conjugation** is the transfer of DNA from a donor to a recipient bacterial cell.
- Once new DNA gets into a bacterial cell by any mechanism, part of it may then integrate into the recipient's chromosome.

Figure 10.22a

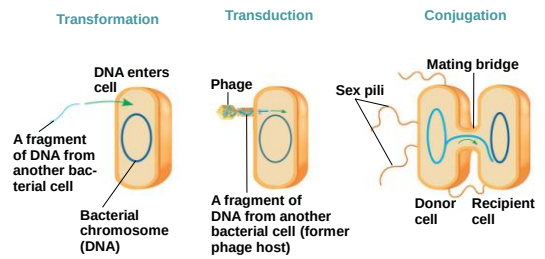
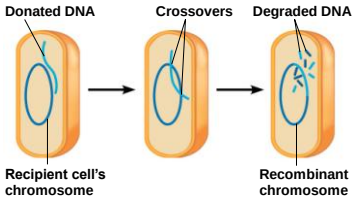


Figure 10.22b

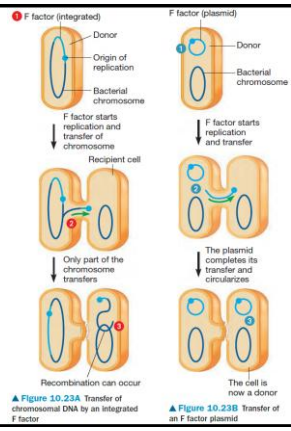
The integration of donated DNA into the recipient cell's chromosome



10.23 Bacterial plasmids can serve as carriers for gene transfer

- The ability of a donor *E. coli* cell to carry out conjugation is usually due to a specific piece of DNA called the **F factor** (f for fertility).
  - An F factor can exist as a **plasmid**, a small, circular DNA molecule separate from the bacterial chromosome.
  - **R plasmids** pose serious problems for human medicine by carrying genes for enzymes that destroy antibiotics.

Checkpoint question Plasmids are useful tools for genetic engineering. Can you guess why?



▲ Figure 10.23A Transfer of chromosomal DNA by an integrated F factor

▲ Figure 10.23B Transfer of an F factor plasmid

Figure 10.23c