The Structure and Replication of Genomes

- **Genetics**
  - Study of inheritance and inheritable traits as expressed in an organism's genetic material

- **Genome**
  - The entire genetic complement of an organism
  - Includes its genes and nucleotide sequences
The Structure of Prokaryotic Genomes

- Prokaryotic Chromosomes
  - Main portion of DNA, along with associated proteins and RNA
  - Prokaryotic cells are *haploid* (single chromosome copy)
  - Typical chromosome is a circular molecule of DNA in the nucleoid
The Structure of Prokaryotic Genomes

- Plasmids
  - Small molecules of DNA that replicate independently
  - Not essential for normal metabolism, growth, or reproduction
  - Can confer survival advantages
  - Many types of plasmids:
    - *Fertility factors*
    - *Resistance factors*
    - *Bacteriocin factors*
    - *Virulence plasmids*
The Structure and Replication of Genomes

• DNA Replication
  • Other Characteristics of Bacterial DNA Replication
    • Bidirectional
    • Gyrases and topoisomerases remove supercoils in DNA
    • DNA is methylated
      • Control of genetic expression
      • Initiation of DNA replication
      • Protection against viral infection
      • Repair of DNA
Figure 7.7 The bidirectionality of DNA replication in prokaryotes.
Gene Function

• The Relationship Between Genotype and Phenotype
  • Genotype
    • Set of genes in the genome
  • Phenotype
    • Physical features and functional traits of the organism
  • Genotype determines phenotype
  • Not all genes are active at all times
Gene Function

• **The Transfer of Genetic Information**
  • Transcription
    • Information in DNA is copied as RNA
  • Translation
    • Polypeptides synthesized from RNA
  • Central dogma of genetics
    • DNA transcribed to RNA
    • RNA translated to form polypeptides
Figure 7.8 The central dogma of genetics.

DNA (genotype)

Transcription

mRNA

Translation by ribosomes

NH₂ — Methionine — Arginine — Tyrosine — Leucine — ... Polypeptide

Phenotype
Figure 7.9 The events in the transcription of RNA in prokaryotes.

1a. RNA polymerase attaches nonspecifically to DNA and travels down its length until it recognizes a promoter sequence. Sigma factor enhances promoter recognition in bacteria.

1b. Upon recognition of the promoter, RNA polymerase unzips the DNA molecule beginning at the promoter.

(a) Initiation of transcription

2. Triphosphate ribonucleotides align with their DNA complements, and RNA polymerase links them together, synthesizing RNA. No primer is needed. The triphosphate ribonucleotides also provide the energy required for RNA synthesis.

(b) Elongation of the RNA transcript

3a. Self-termination: transcription of GC-rich terminator region produces a hairpin loop, which creates tension, loosening the grip of the polymerase on the DNA.

3b. Rho-dependant termination: Rho pushes between polymerase and DNA. This causes release of polymerase, RNA transcript, and Rho.

(c) Termination of transcription: release of RNA polymerase
Figure 7.11 Processing eukaryotic mRNA.

Exons (polypeptide coding regions)

Introns (noncoding regions)

Transcription

Processing

Spliceosomes

mRNA splicing

mRNA (codes for one polypeptide)

Nucleoplasm

Nuclear envelope

Nuclear pore

Cytosol

mRNA
Gene Function

- **Translation**
  - Events in Translation
    - Three stages of translation:
      - *Initiation*
      - *Elongation*
      - *Termination*
  - All stages require additional protein factors
  - Initiation and elongation require energy (GTP)
Translation: The Process
Gene Function

- **Regulation of Genetic Expression**
  - Most genes are expressed at all times
  - Other genes transcribed and translated when cells need them
    - Allows cell to conserve energy
  - Regulation of polypeptide synthesis:
    - Typically halts transcription
    - Can stop translation directly
Mutations of Genes

• **Mutation**
  • Change in the nucleotide base sequence of a genome
  • Rare event
  • Almost always deleterious
  • Rarely leads to a protein that improves ability of organism to survive
Figure 7.24 The effects of the various types of point mutations.

(a) Normal

Normal DNA: A A A A T A C G T G C A
Normal mRNA: U U U U A U G C A C G U
Normal polypeptide: Phe Tyr Ala Arg

(b) Silent mutation

Mutated DNA strand: A A G A T A C G T G C A
Mutated mRNA: U U C U A U G C A C G U
No change in amino acid sequence of polypeptide

(c) Missense mutation

Mutated DNA strand: A A A A T A C C T G C A
Mutated mRNA: U U U U A U G G A C G U
Slightly different amino acid sequence

(d) Nonsense mutation

Mutated DNA strand: A A A A T T C G T G C A
Mutated mRNA: U U U U A G C A C G U
Phe STOP CODON
Polypeptide synthesis ceases

Frameshift mutations:

(e) Frameshift insertion

Insertion
Mutated DNA strand: A A A A T A T A C G T G C A
Mutated mRNA: U U U A U A U G C A C G U
Phe Ile Cys Thr
Major difference in amino acid sequence

(f) Frameshift deletion

Mutated DNA strand: A A A A A C G T G C A
Mutated mRNA: U U U U U U G C A C G U
Phe Leu His Val
Major difference in amino acid sequence
Mutations of Genes

- **Mutagens**
  - Radiation
    - Ionizing radiation
    - Nonionizing radiation
  - Chemical mutagens
    - Nucleotide analogs
      - Disrupt DNA and RNA replication
      - Nucleotide-altering chemicals
        - Result in base-pair substitutions and missense mutations
    - Frameshift mutagens
      - Result in nonsense mutations
Mutations of Genes

• **Frequency of Mutation**
  • Mutations are rare events
    • Otherwise organisms could not effectively reproduce
  • Mutagens increase the mutation rate by a factor of 10 to 1000 times
Genetic Recombination and Transfer

• **Vertical gene transfer**
  - Organisms replicate their genomes and provide copies to descendants

• **Horizontal Gene Transfer Among Prokaryotes**
  - Horizontal gene transfer
    - Donor cell contributes part of genome to recipient cell
  - Three types:
    - Transformation
    - Transduction
    - Bacterial conjugation
Figure 7.33 Transformation of *Streptococcus pneumoniae*.

**Observations of *Streptococcus pneumoniae***

- **Live cells**
  - Injection → Mouse dies

- **Heat-treated dead cells of strain S**
  - Injection → Mouse lives

- **Strain R live cells (no capsule)**
  - Injection → Mouse lives

**Griffith's experiment:**

- **Living strain R** + **Heat-treated dead cells of strain S**
  - Injection → Mouse dies
  - Culture of *Streptococcus* from dead mouse
    - Living cells with capsule (strain S)
  - DNA broken into pieces
    - Some cells take up DNA from the environment and incorporate it into their chromosomes
    - Transformed cells acquire ability to synthesize capsules

**In vitro transformation**

- **Heat-treated dead cells of strain S**
  - DNA fragment from strain S
  - Living strain R
  - Some cells take up DNA from the environment and incorporate it into their chromosomes
  - Transformed cells acquire ability to synthesize capsules
Figure 7.34 Transduction.

**Cell 1**
- Bacteriophage
- Host bacterial cell (donor cell)
- Bacterial chromosome

1. Phage injects its DNA.
2. Phage enzymes degrade host DNA.
3. Cell synthesizes new phages that incorporate phage DNA and, mistakenly, some host DNA.

Transducing phage

**Cell 2**
- Recipient host cell

4. Transducing phage injects donor DNA.
5. Donor DNA is incorporated into recipient’s chromosome by recombination.
Donor cell attaches to a recipient cell with its pilus.

Pilus draws cells together.

One strand of F plasmid DNA transfers to the recipient.

The recipient synthesizes a complementary strand to become an F+ cell with a pilus; the donor synthesizes a complementary strand, restoring its complete plasmid.
Deadly Horizontal Gene Transfer

- Patient Details?
- What infection? MDR?
- Define healthcare-associated infection
- Source of the infection?
- Three ways by which Enterococcus faecium might have acquired genes for drug resistance.
- How can hospital personnel prevent the spread of resistant E. faecium throughout the hospital?