Advanced Cell Biology. Lecture 17

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Outline

DNA reparation (end)

DNA recombination

Mobile elements

Outline

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DNA reparation (end)

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Mobile elements

Previous final question: the answer

What is the difference between deletion and substitution?

Previous final question: the answer

What is the difference between deletion and substitution?

- Deletion is nucleotide **removal** whereas substitution in nucleotide *replacement*
- What is the third variant?

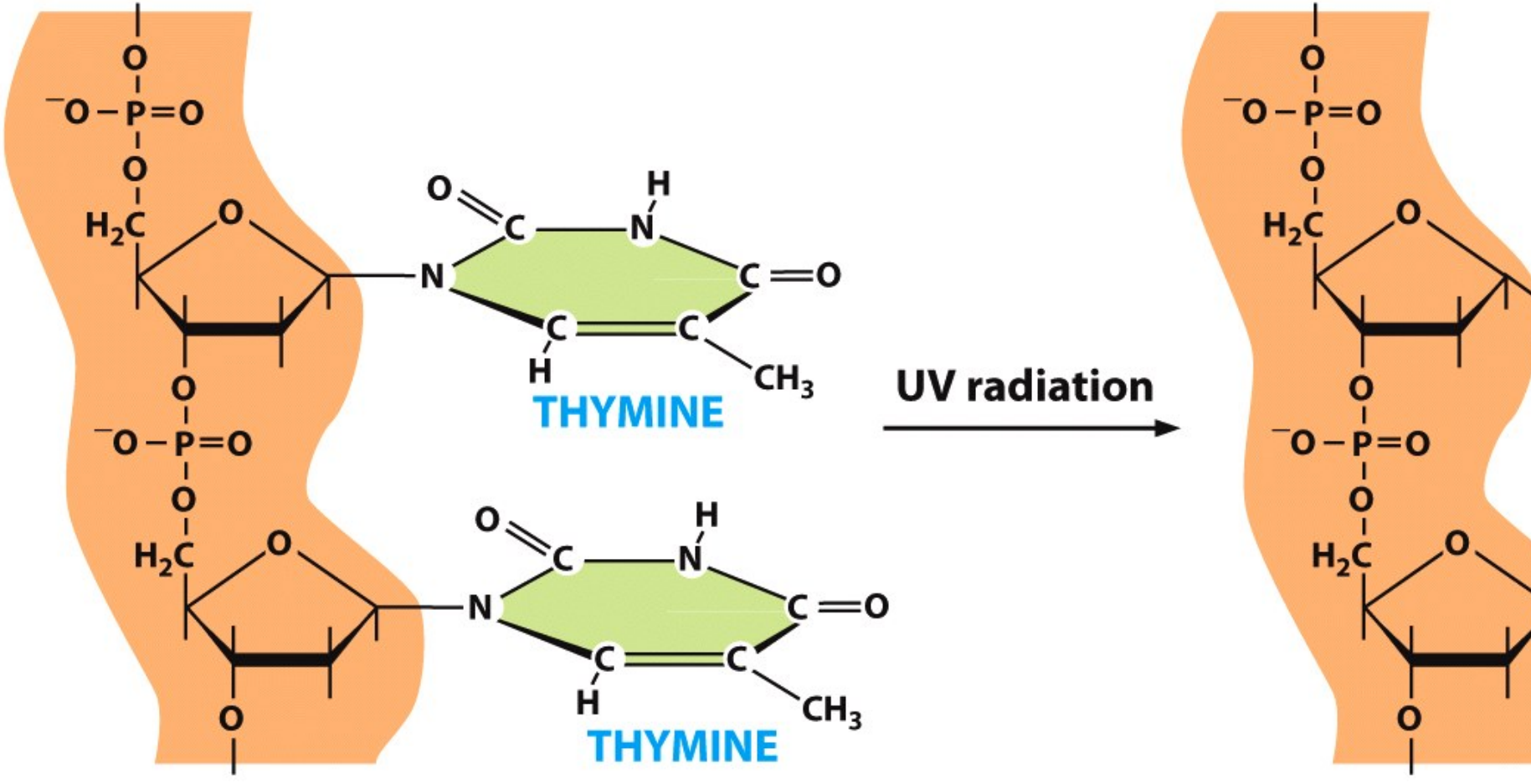
Lab 4 schedule

- 1 pm section:
  1. Avery et al. (1944). Murray, Heitkamp, Namanny
  2. Watson & Crick (1953): 2 papers. **Simons**, Wolfe, Rosin, Evanoff
  3. Wilkins et al. (1953). Wagner, Eaton, Bauer, Morse
- 3 pm section:
  1. Avery et al. (1944). **Beyer K.**, Beyer Sh., Elder, Coffin, Rohlk, Glaspie
  2. Watson & Crick (1953): 2 papers. **Wilson**, Clark, DesRoches, Bruckhard, Aguilar
  3. Wilkins et al. (1953). Davis, **Kaur**, Gilles, Yates

Pyrimidine dimers

- UV radiation often results in forming of pyrimidine (T or C) dimers
- Dimers will stop DNA replication and transcription
- The final result is often a melanoma type of skin cancer

Pyrimidine dimers



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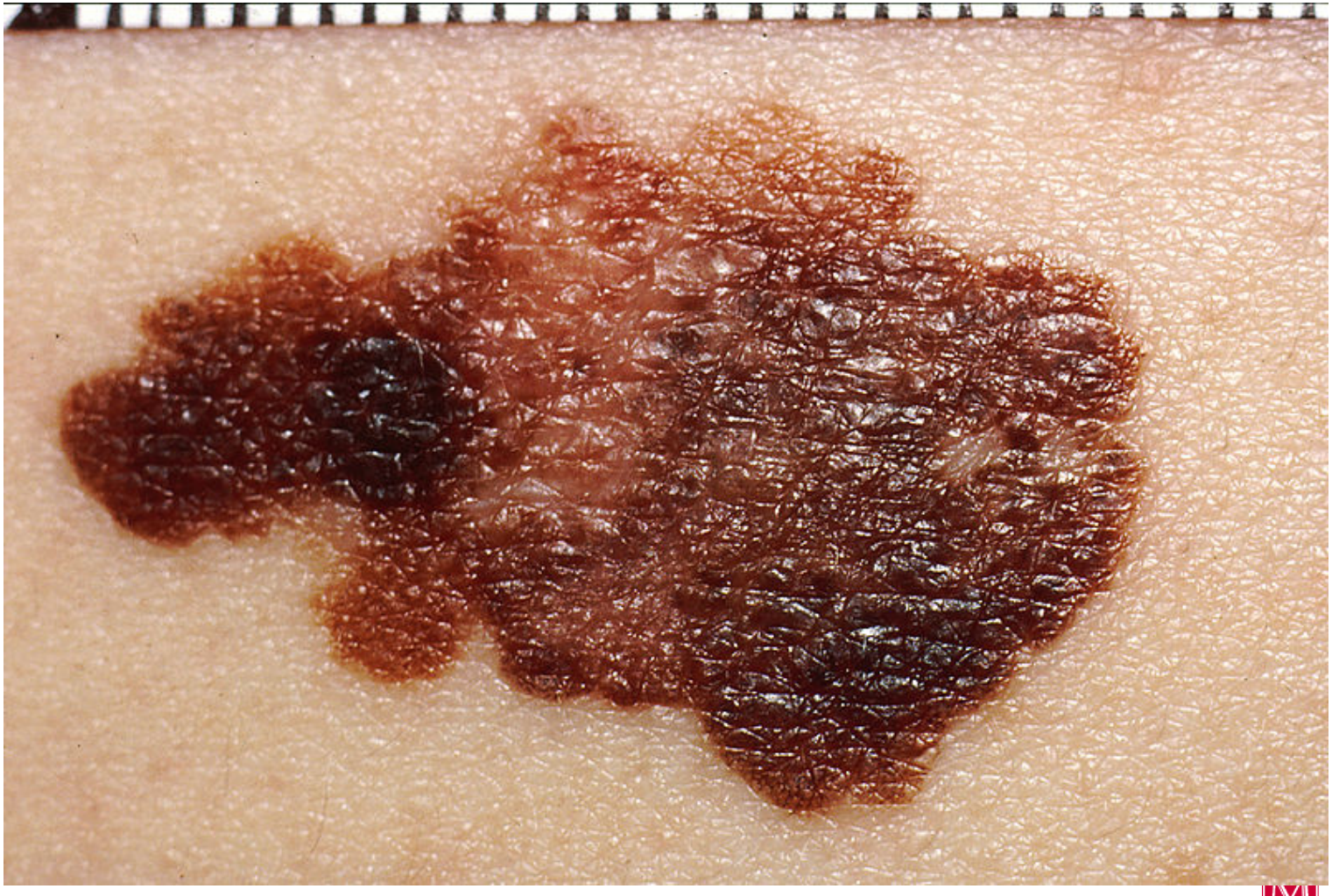
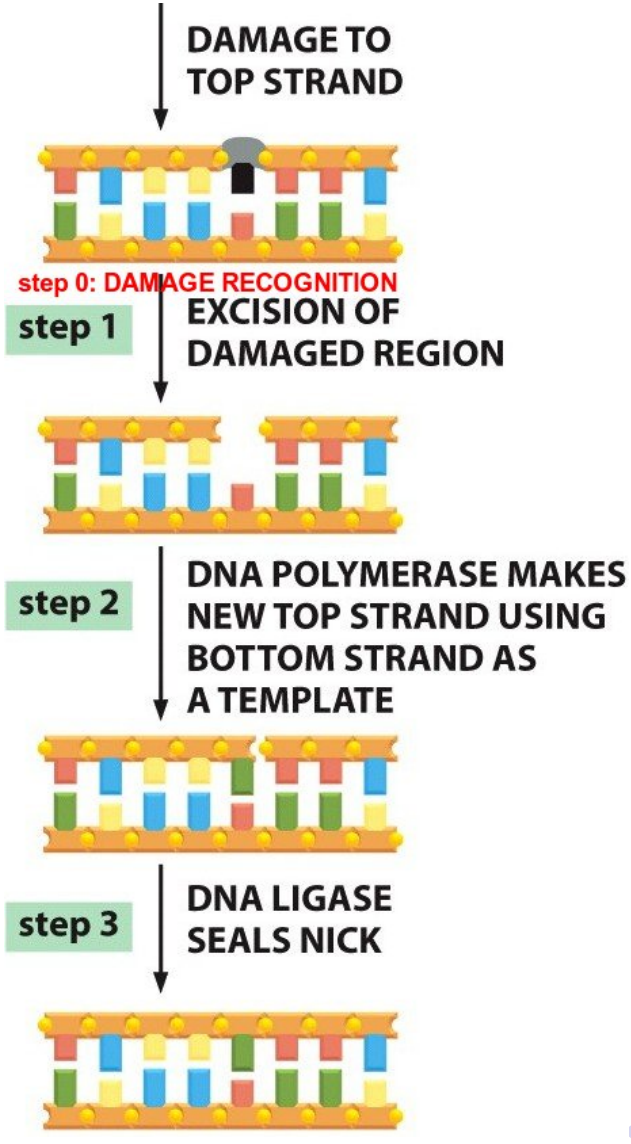
Skin melanoma



Basic way of DNA repair

1. Damage recognition
2. Excision
3. Resynthesis
4. Ligation

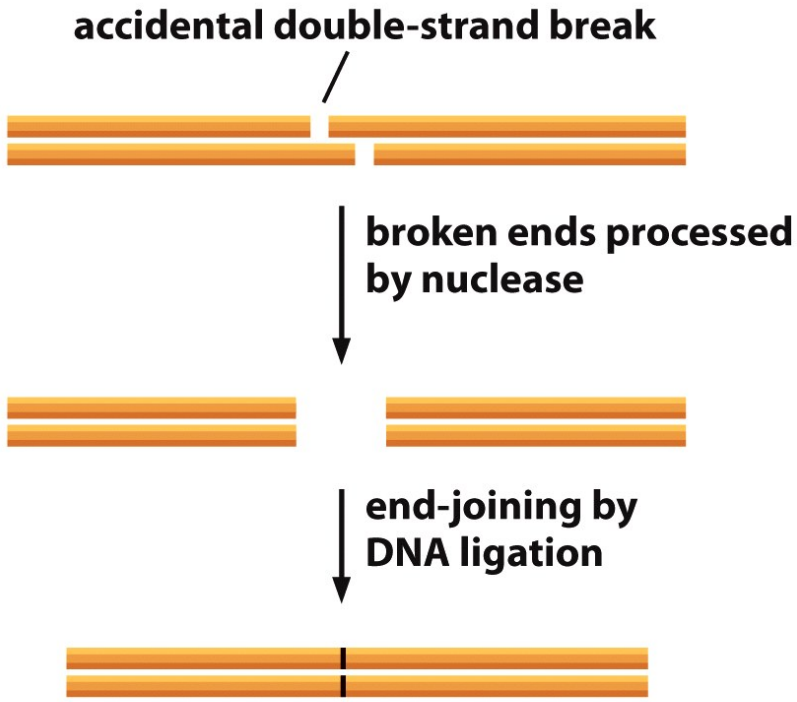
DNA repair flow



Nonhomologous end-joining

- The quick-and-dirty mechanism of reparation when both strands are broken
- The reparation will result in deletion

Nonhomologous end-joining



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Homologous recombination/reparation

- Occur between two different DNA duplexes
- Uses the availability of homologous copies of DNA (e.g., homologous chromosomes)
- Requires breakage of both DNA strands

Homologous reparation, part I

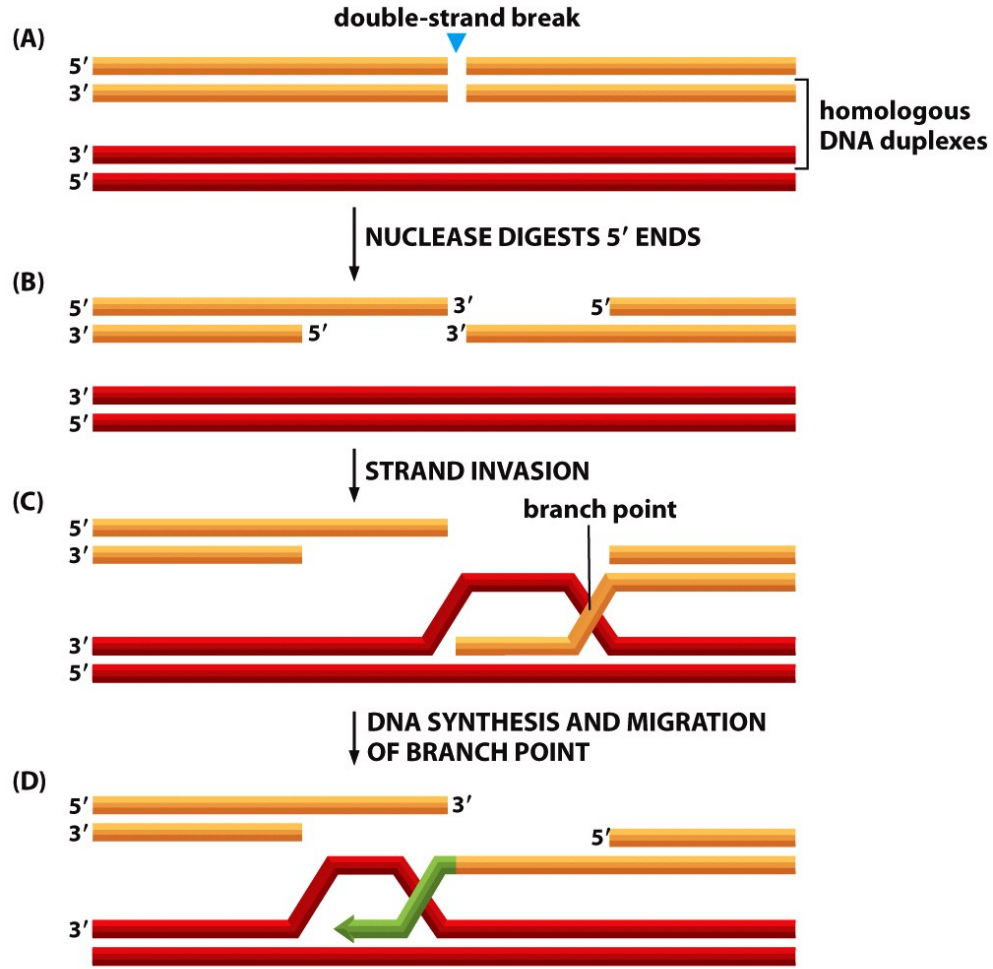

Figure 6-29 part 1 of 2 Essential Cell Biology 3/e (© Garland Science 2010)

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Homologous reparation, part II

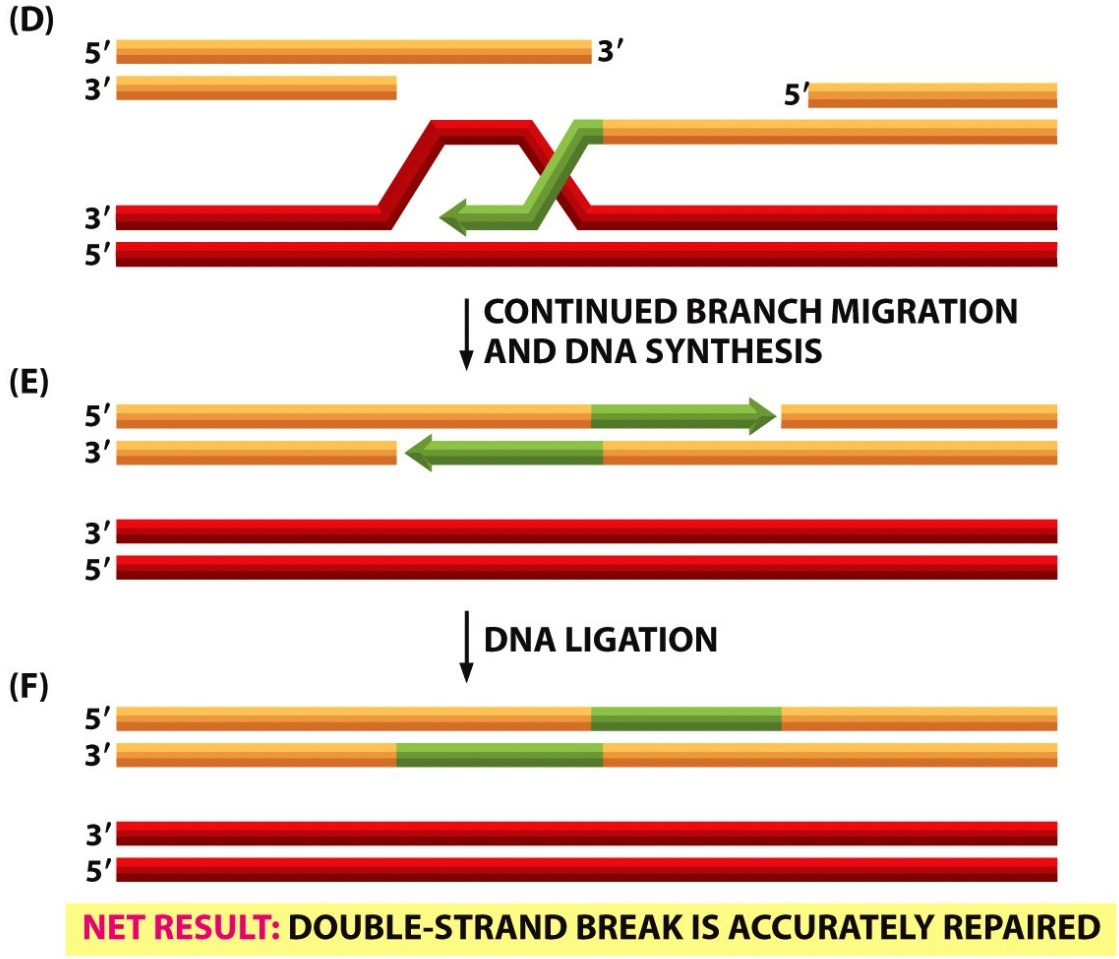


Figure 6-29 part 2 of 2 Essential Cell Biology 3/e (© Garland Science 2010)

Branch point and invading strand

- Enzymes take off two DNA chunks from each strand of one duplex
- *Invading strand* will cross with the strand of other duplex
- Place of crossing between two DNA strands from different duplexes is a *branch point*
- Process is finished with DNA ligation

Holliday junctions in meiosis

- In meiosis prophase, DNA duplexes are crossing and changing parts in the way similar to homologous reparation
- Two resulted strands will contain newly synthesized fragments, and all four will cross to form a hybrid molecules

Recombination, part I

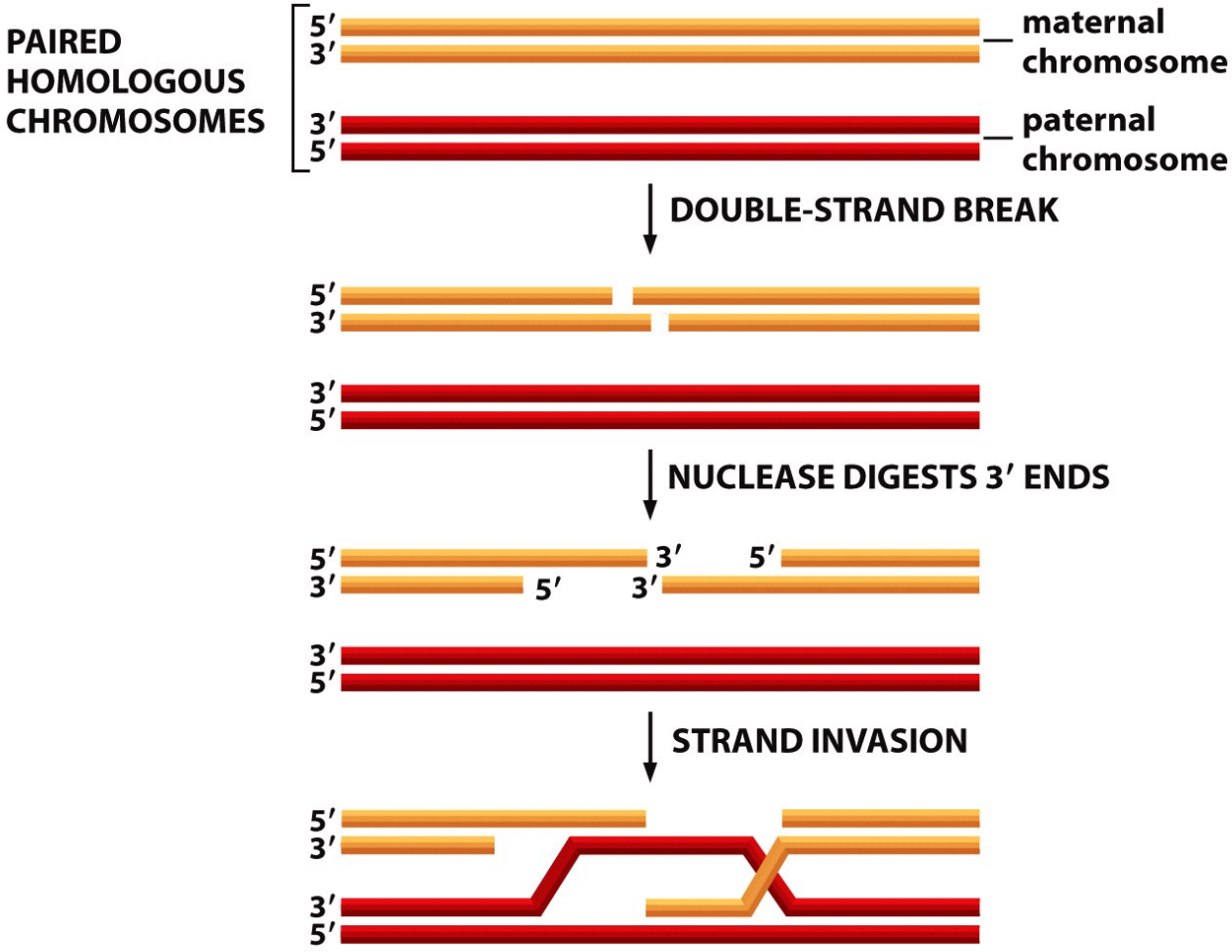
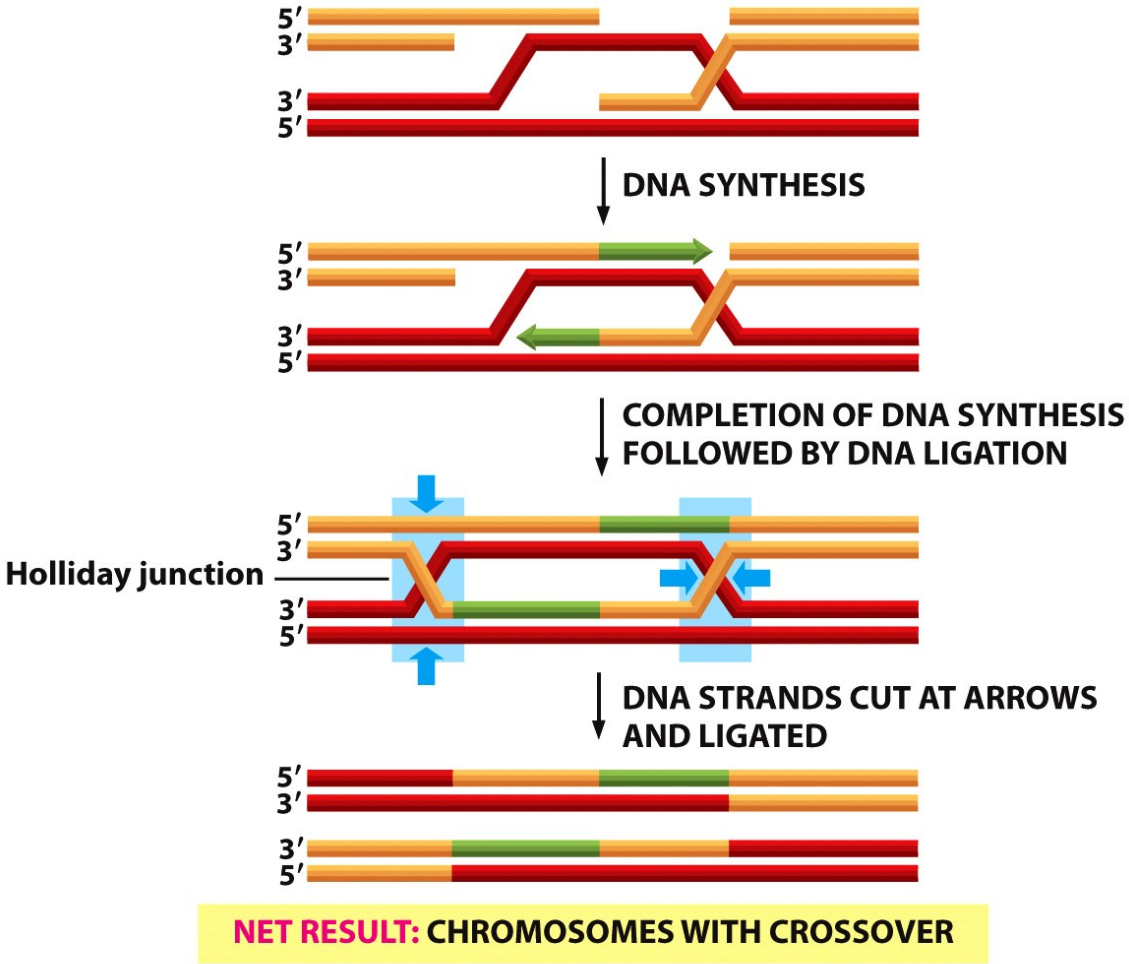


Figure 6-31 part 1 of 2 Essential Cell Biology 3/e (© Garland Science 2010)

Recombination, part II



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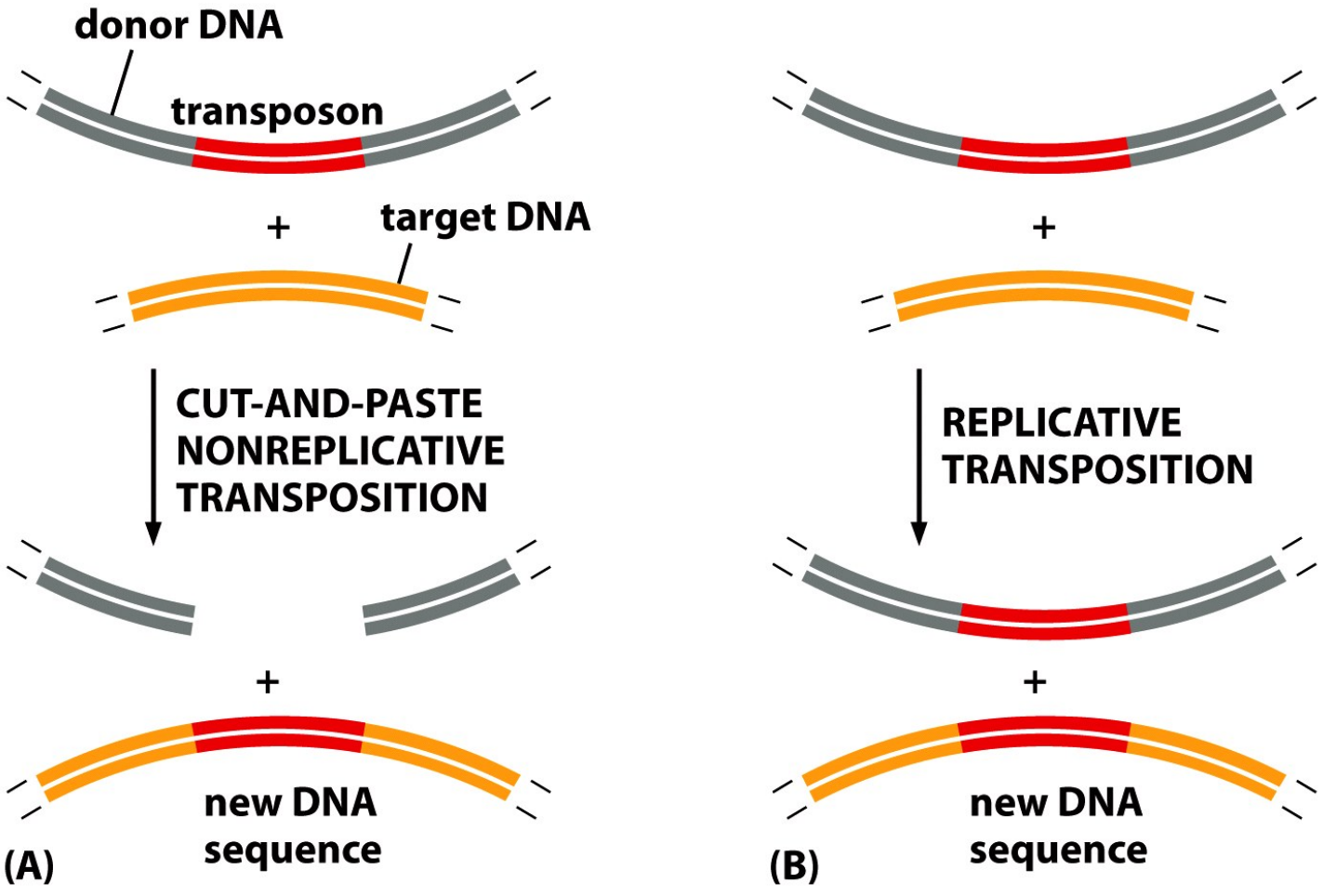
Recombination movie

Recombination through mobile elements

- Some parts of DNA molecules can migrate between duplexes, they are transposons
- DNA-only transposons may be cut and pasted (migrate), or replicate across DNA duplexes
- Some transposons replicate through RNA with the help of reverse transcriptase—retrotransposons

DNA only transposons



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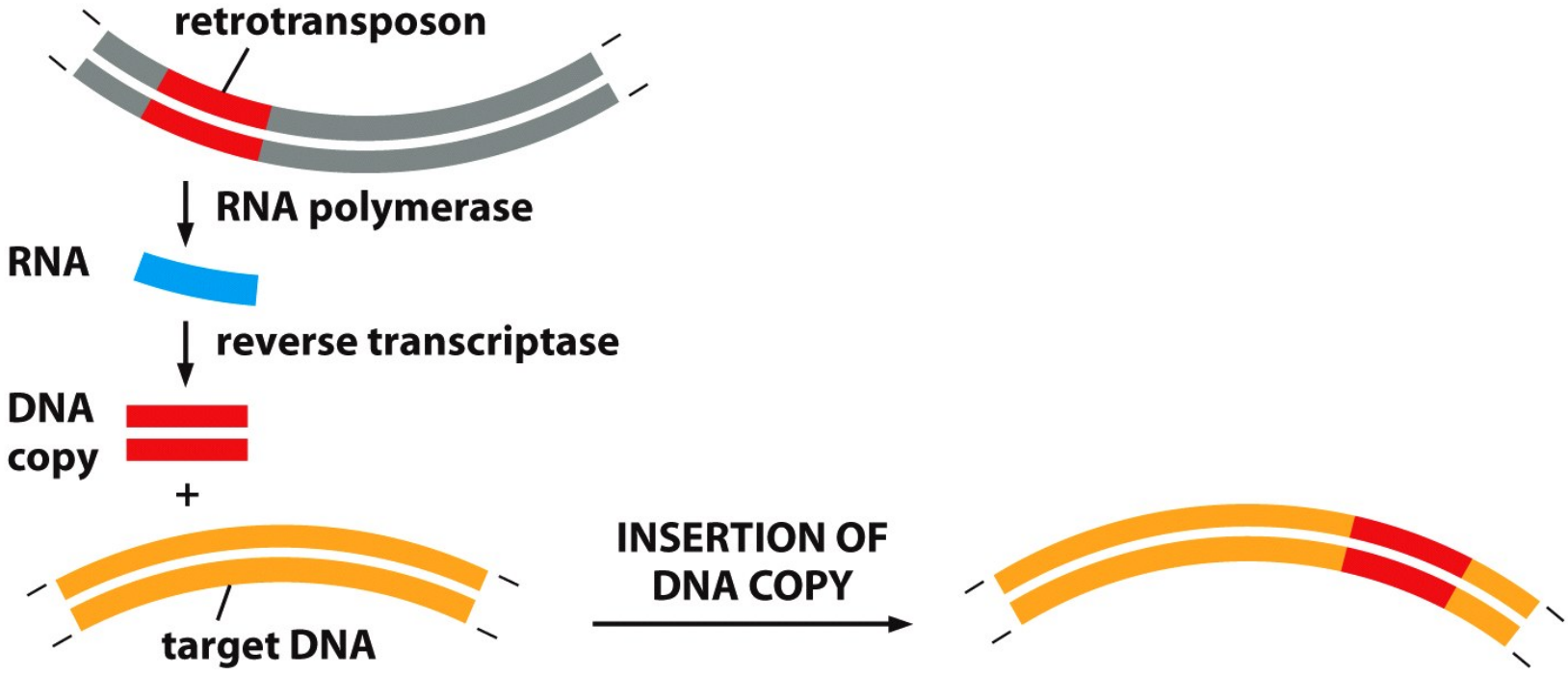
Retrotransposon



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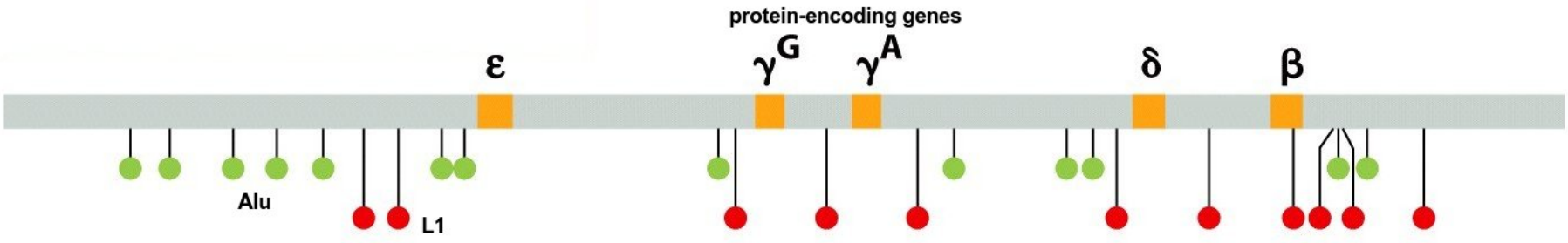
Human retrotransposons

- Long *L1 elements* (15% of human genome) encode reverse transcriptase themselves
- Short *Alu elements* (11% of genome) depend on external enzymes

Human retrotransposons



Alu sequence

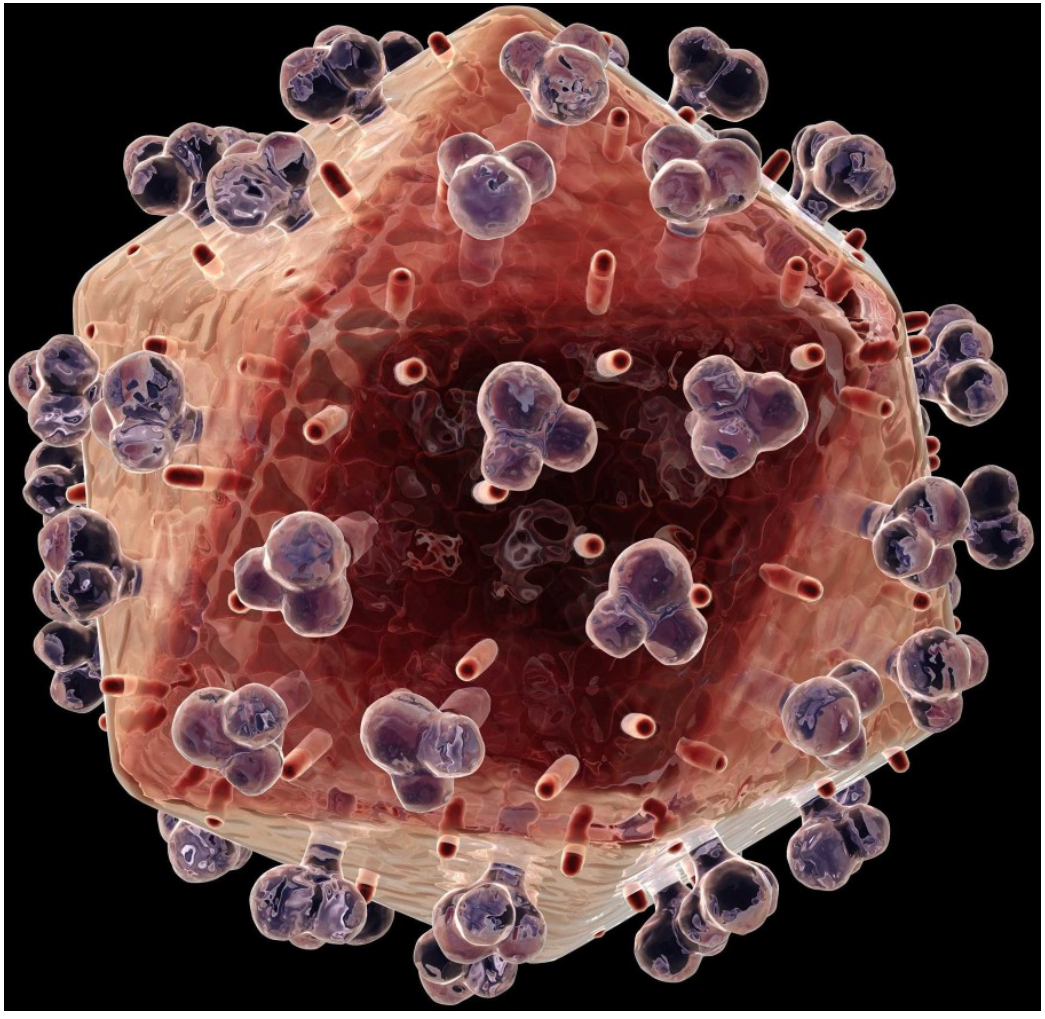
GCCGGGCGCGGTGGCGCGTGCCTGTAGTCCC**AGCT**ACTCG
GGAGGCTGAGGCTGGAGGATCGCTTGAGTCCAGGAGTTCTGGGCT
GTAGTGCGCTATGCCGATCGGGTGTCCGCACTAAGTTCGGCATCA
ATATGGTGACCTCCCGGGAGCGGGGGACCACCAGGTTGCCTAAGGA
GGGGTGAACCGGCCCAGGTCGGAAACGGAGCAGGTCAAAACTCCC
GTGCTGATCAGTAGTGGGATCGCGCCTGTGAATAGCCACTGCACTC
CAGCCTGGGCAACATAGCGAGACCCCGTCTCT

AGCT is the *recognition site*

Viruses and retroviruses

- If transposon acquires the protein shell (capsid) and goes outside cell, it becomes a virus
- Retroviruses (like HIV) use reverse transcriptase and may even insert themselves into cell DNA for a while

HIV retrovirus



Final question (2 points)

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What is better for the cell, nonhomologous or homologous reparation? Why?

Summary

- DNA suffers from multiple damaging events; multiple reparation systems are trying to lower mutation risks
- Homologous recombination is used when two similar DNA duplexes (homologous DNAs) are available
- Viruses are transposons escaped from cells

For Further Reading

A. Shipunov.
Advanced Cell Biology [Electronic resource].
2011—onwards.
Mode of access: `http://ashipunov.info/shipunov/school/biol_250`

B. Alberts et al.
Essential Cell Biology. 3rd edition.
Garland Science, 2009.
Chapter 7.