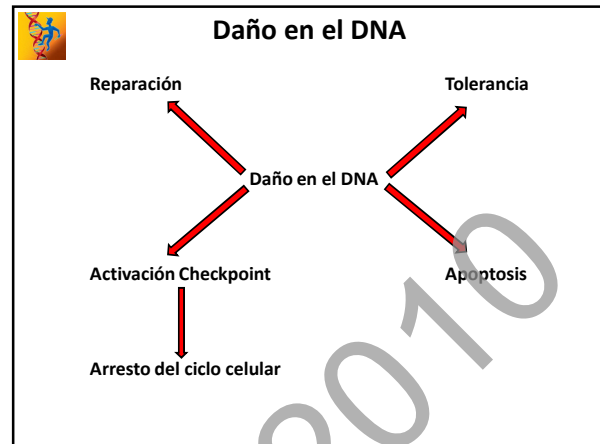




Reparación de DNA

Dra. Jennifer Alcaíno G
Septiembre de 2010



Causas daño en el DNA

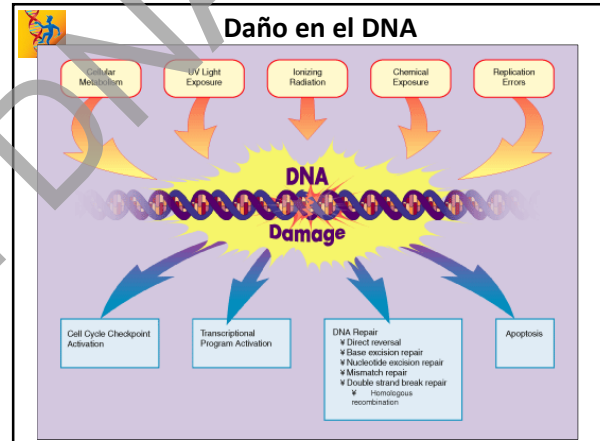
Metabolismo celular:
Propiedades de las bases nitrogenadas
Metabolismo Oxidativo.

Errores en la replicación del DNA.

Errores en la reparación del DNA.

Mutágenos ambientales:

Físicos
Químicos



Tipos de Reparación DNA

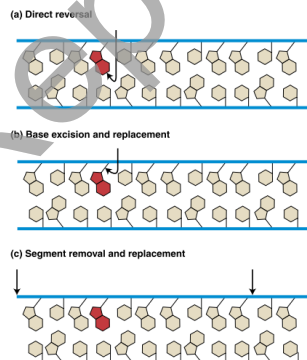
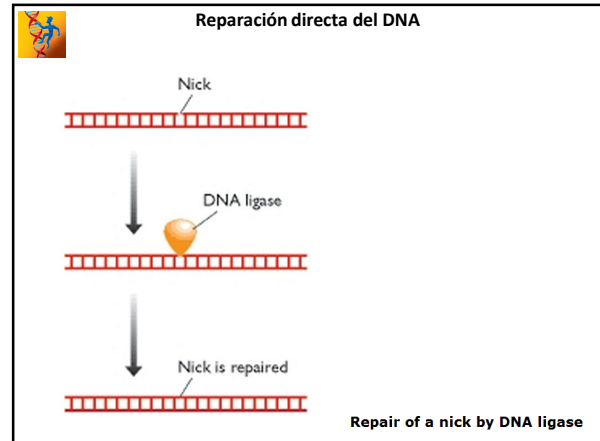
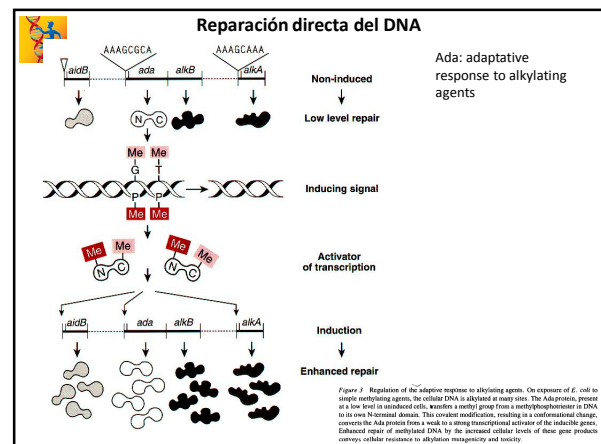
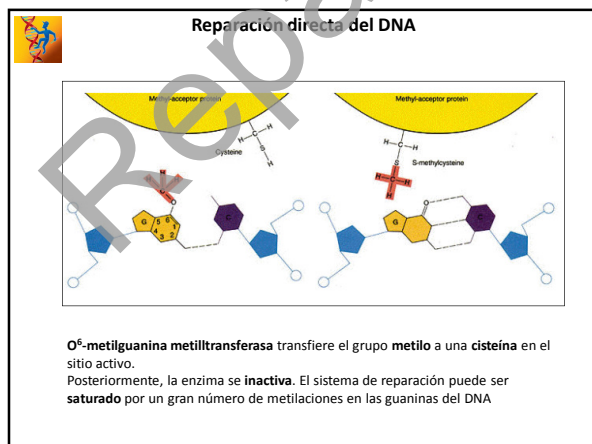
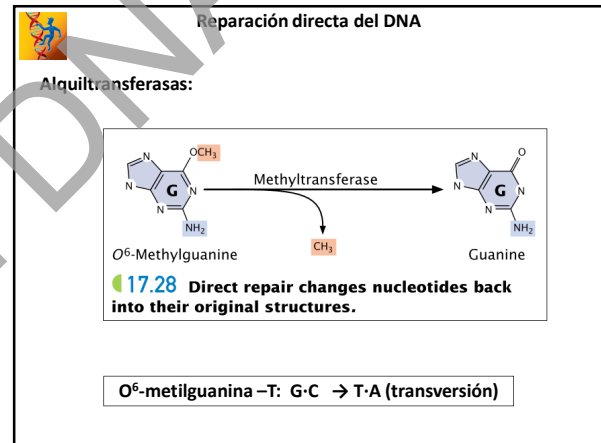
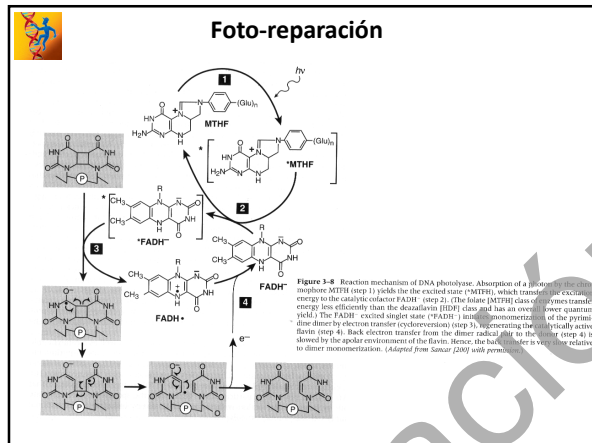
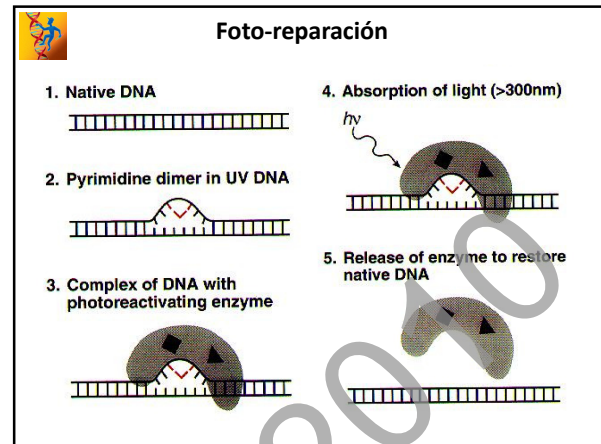
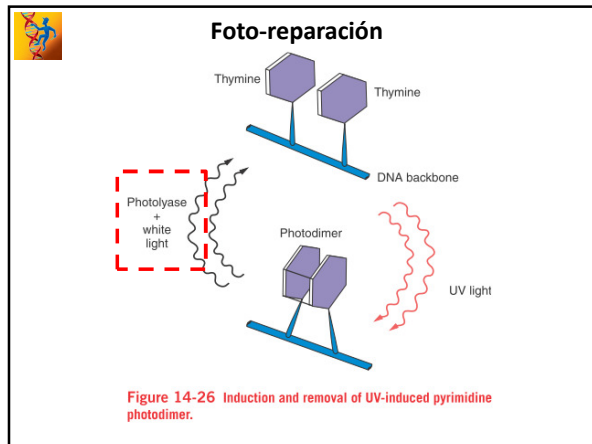


Figure 14-25 Three types of repair of DNA with a damaged base.

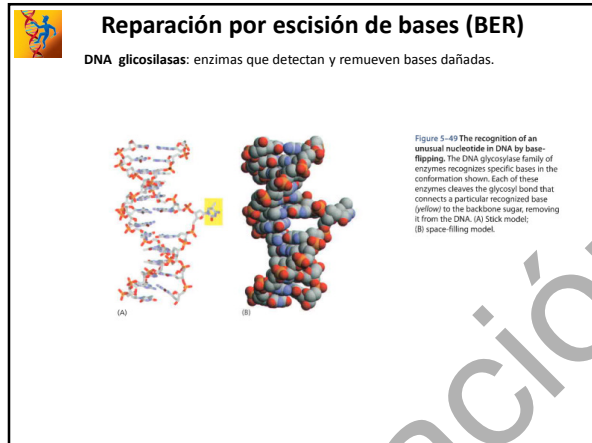
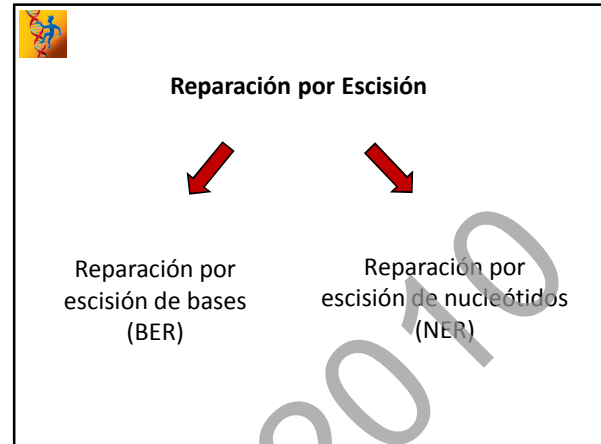




Reparación directa del DNA

Table 1 Inducible genes of the adaptive response to alkylation damage

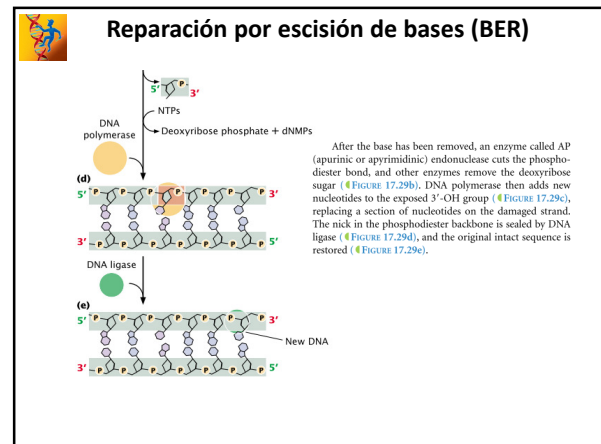
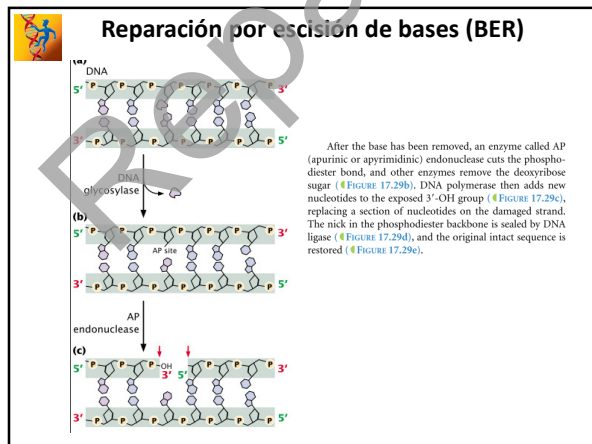
Inducible gene	Chromosomal location	Mutant phenotype	Gene product	Lesions repaired	Other properties
<i>ada</i>	47'	Sensitive to mutagenesis and killing	39-kd DNA methyltransferase	O ⁶ MeG O ⁴ MeT p(Me)	Positive regulator of adaptive response
<i>alkB</i>	47'	Sensitive to killing	24-kd protein	?	—
<i>alkA</i>	45'	Sensitive to killing	31-kd DNA glycosylase	3MeA 3MeG O ⁶ MeC O ⁶ MeT	—
<i>aidB</i>	95'	Resistant to killing	?	—	—

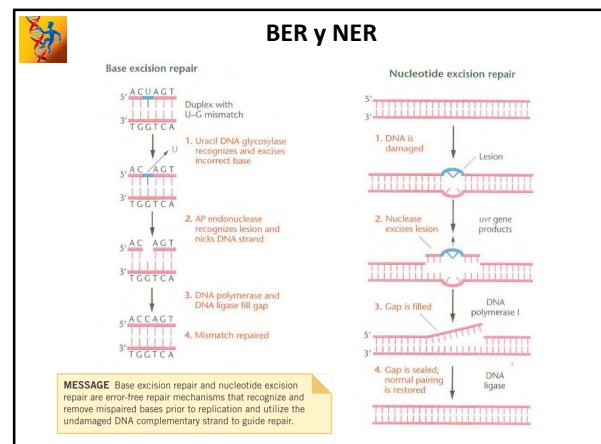
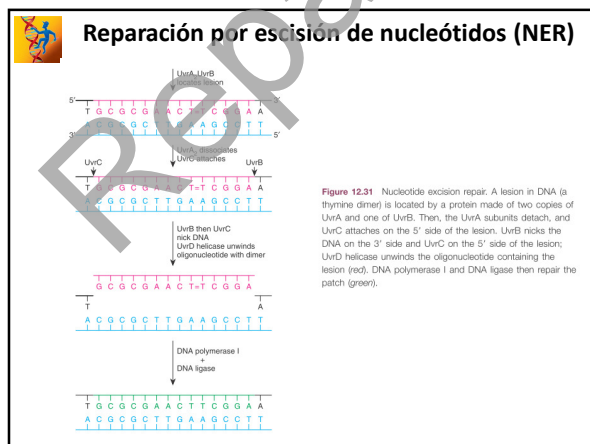
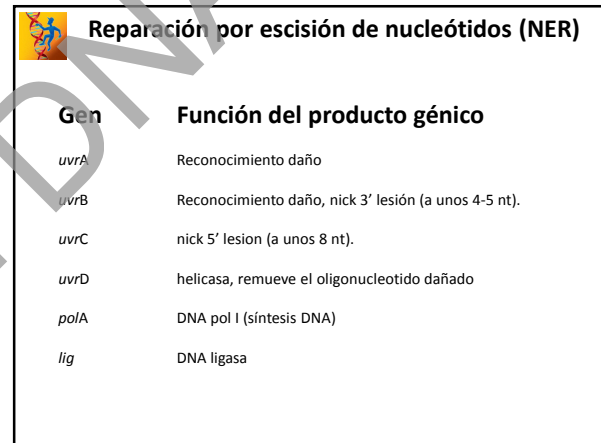
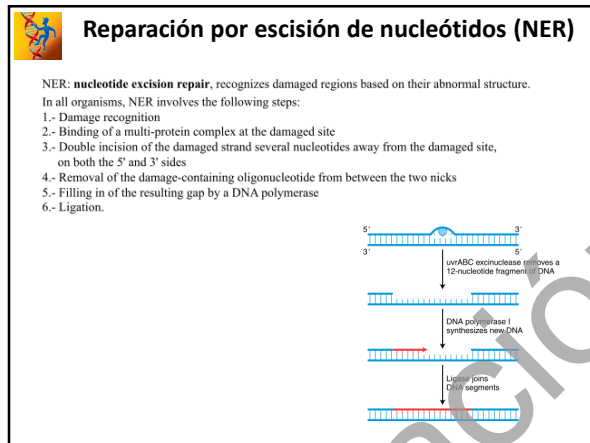
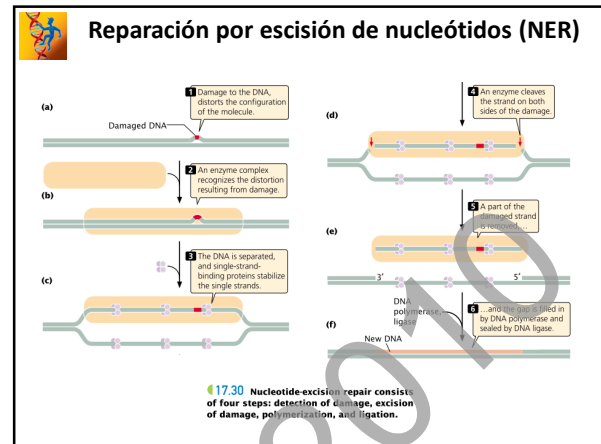
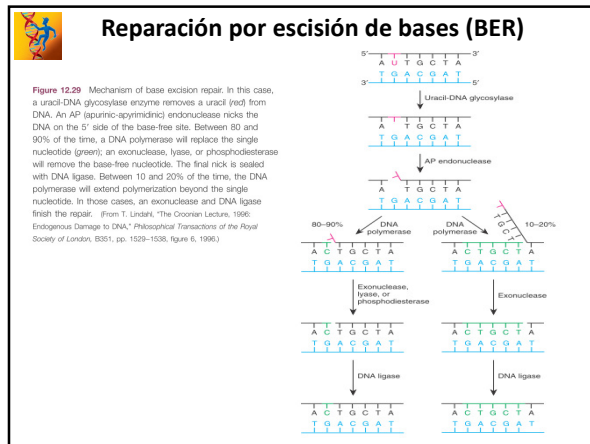


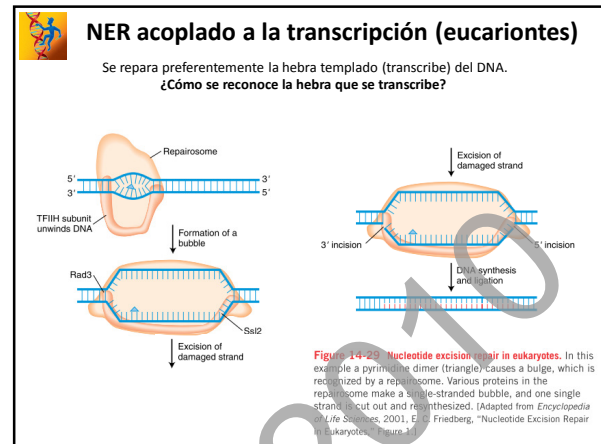
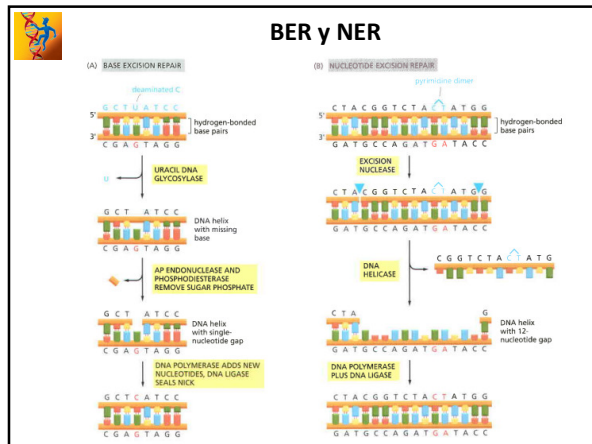
Reparación por escisión de bases (BER)

Table 4-2 DNA glycosylases

Enzyme	Substrate	Products
Uvr-DNA glycosylase	DNA containing uracil	Uracil + AP sites
Uvr-DNA glycosylase	DNA containing hydroxymethyluracil	Hydroxymethyluracil + AP sites
5-mC-DNA glycosylase	DNA containing 5-methylcytosine	5-methylcytosine + AP sites
8-oxo-DNA glycosylase	DNA containing 8-oxoguanine	8-oxoguanine + AP sites
Thymine mismatch-DNA glycosylase	DNA containing G-T mispairs	Thymine + AP sites
Mut-DNA glycosylase	DNA containing G-A mispairs	Adenine + AP sites
3-mA-DNA glycosylase I	DNA containing 3-methyladenine	3-Methyladenine + AP sites
3-mA-DNA glycosylase II	DNA containing 3-methyladenine, 7-methyladenine, 7-methylguanine, or 3-methylguanine	3-Methyladenine, 7-methyladenine, 7-methylguanine, or 3-methylguanine + AP sites
Fapy-DNA glycosylase	DNA containing formamidopyrimidine nucleotides, or 8-hydroxyguanine	2,6-Diamino-4-hydroxy-5,6-dihydro-2H-pyrimidin-4-one + AP sites
5,6-Hf-DNA glycosylase (endonuclease III)	DNA containing 5,6-hydroxylated thymine residues	5,6-Hydroxylated thymine + AP sites
FD-DNA glycosylase	DNA containing pyrimidine dimers	Pyrimidine dimers in DNA with hydrolyzed 5' glycosyl bonds + AP sites







Reparación por escisión de nucleótidos (NER)

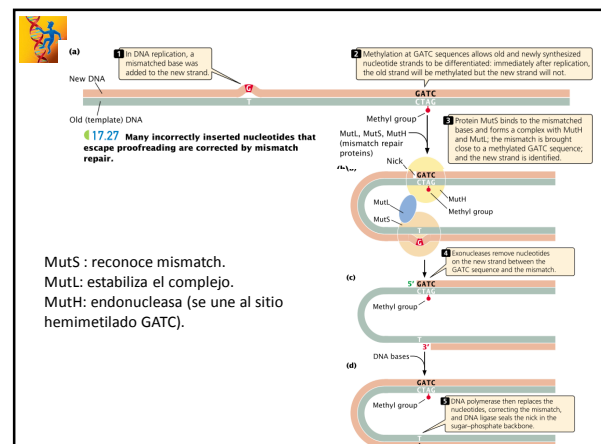
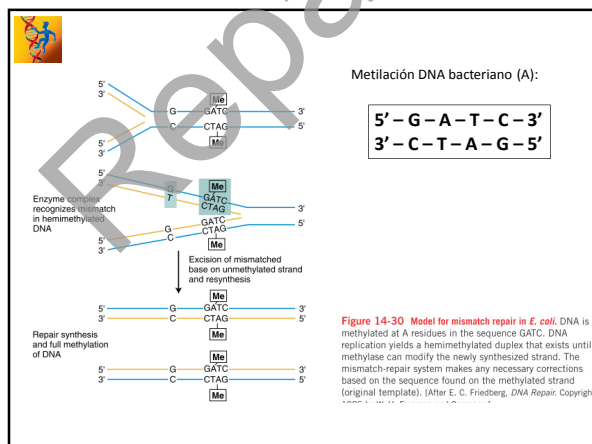
Sunlight includes a strong UV component so exposure to sunlight produces pyrimidine dimers in the DNA of skin cells. Although human cells lack photolyase (the enzyme that repairs pyrimidine dimers in bacteria), most pyrimidine dimers in humans can be corrected by nucleotide excision repair. However, the cells of most people with xeroderma pigmentosum are defective in nucleotide excision repair, and many of their pyrimidine dimers go uncorrected and may lead to cancer.

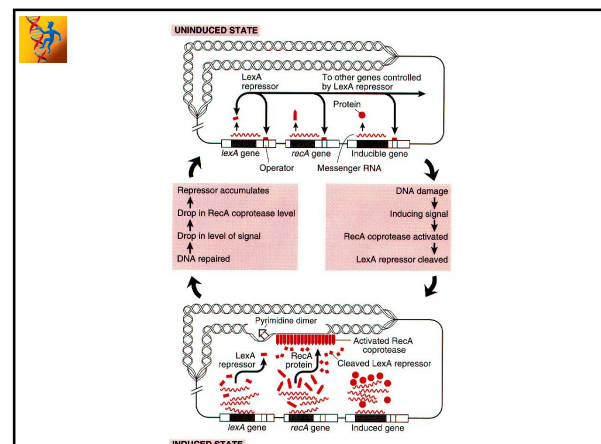
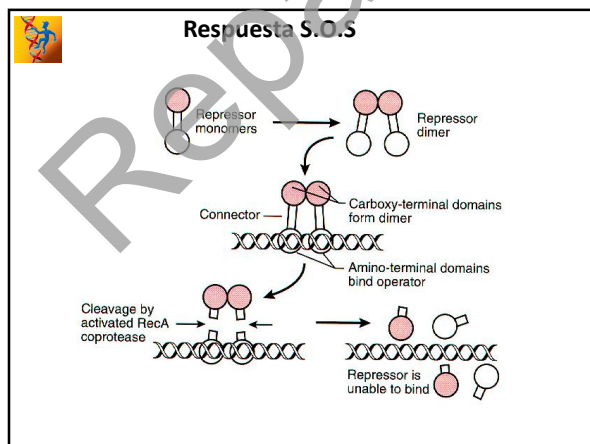
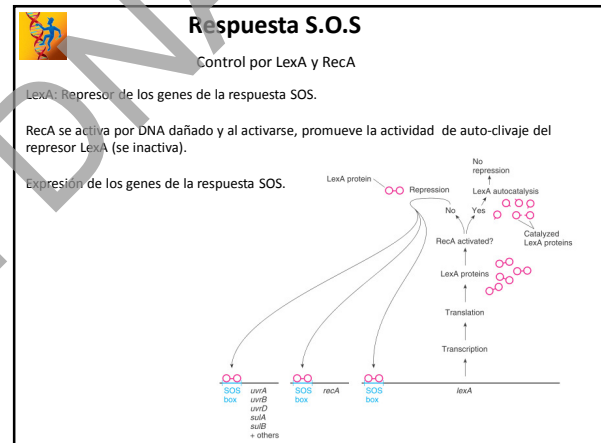
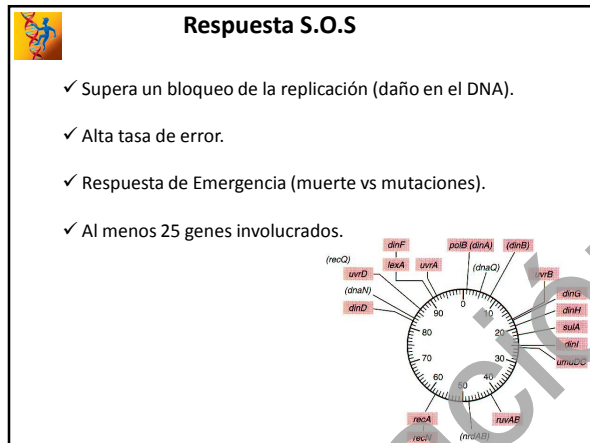
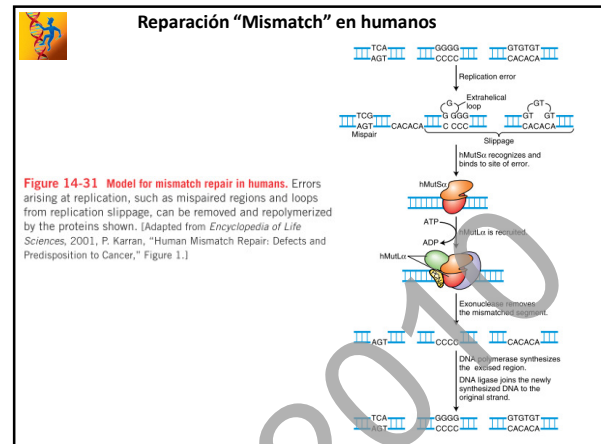
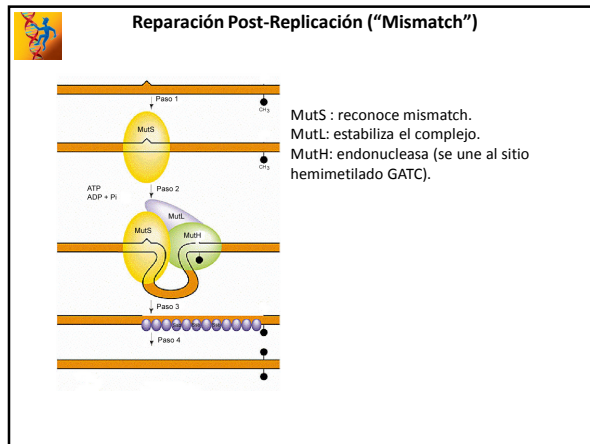
17.31 Xeroderma pigmentosum is a human disease that results from defects in DNA repair.
(Ken Greer/Visuals Unlimited.)

Reparación Post-Replicación ("Mismatch")

1. Reconocer el mal apareamiento.
2. Determinar cual base es la incorrecta.
3. Eliminar el incorrecto y reparar.

- ✓ Frecuencia de mal apareamiento en el DNA: 10^{-4} a 10^{-5} (considerando actividad correctora de DNA pol III).
- ✓ Reparación Mismatch reconoce bases mal apareadas en el DNA (ej. G-T or A-C).
- ✓ ~ 99 % de la reparación en el DNA ocurre por esta vía.





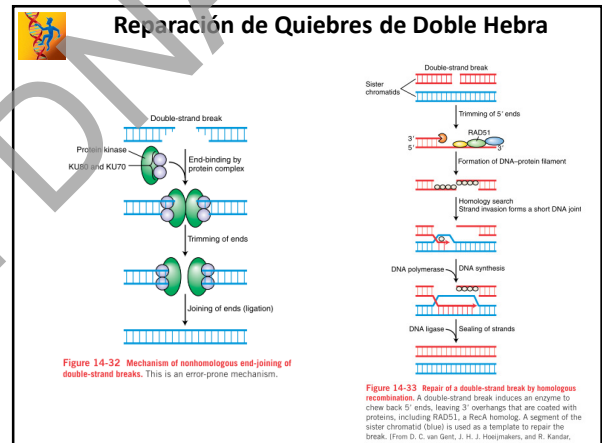
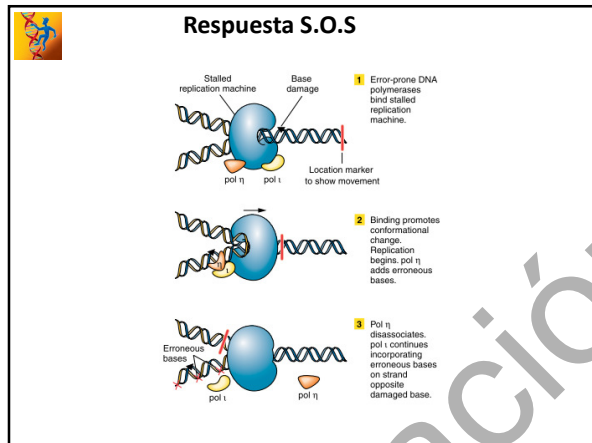
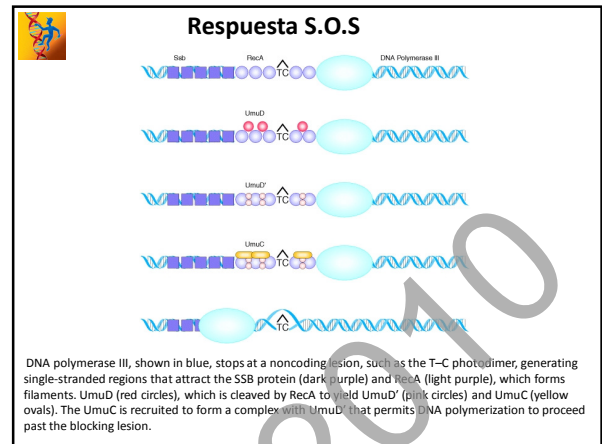
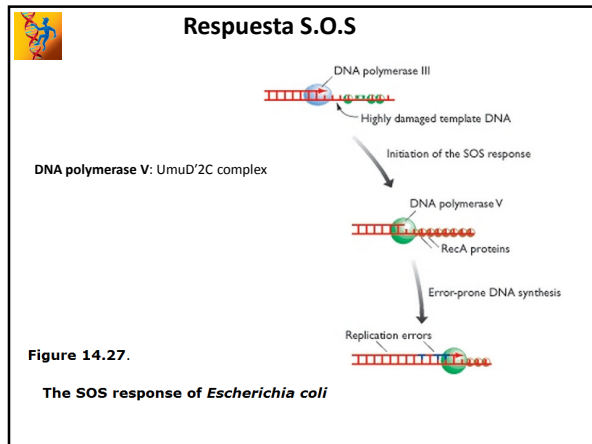


Table 17.6 Genetic diseases associated with defects in DNA repair systems

Disease	Symptoms	Genetic Defect
Xeroderma pigmentosum	Freckle-like spots on skin, sensitivity to sunlight, predisposition to skin cancer	Defects in nucleotide-excision repair
Gockayne syndrome	Dwarfism, sensitivity to sunlight, premature aging, deafness, mental retardation	Defects in nucleotide-excision repair
Trichothiodystrophy	Brittle hair, skin abnormalities, short stature, immature sexual development, characteristic facial features	Defects in nucleotide-excision repair
Hereditary nonpolyposis colon cancer	Predisposition to colon cancer	Defects in mismatch repair
Fanconi anemia	Increased skin pigmentation, abnormalities of skeleton, heart, and kidneys, predisposition to leukemia	Possibly defects in the repair of interstrand cross-links
Ataxia telangiectasia	Defective muscle coordination, dilation of blood vessels in skin and eyes, immune deficiencies, sensitivity to ionizing radiation, predisposition to cancer	Defects in DNA damage detection and response
Li-Fraumeni syndrome	Predisposition to cancer in many different tissues	Defects in DNA damage response

Table 17.5 Summary of common DNA repair mechanisms

Repair System	Type of Damage Repaired
Mismatch	Replication errors, including mispaired bases and strand slippage
Direct	Pyrimidine dimers; other specific types of alterations
Base-excision	Abnormal bases, modified bases, and pyrimidine dimers
Nucleotide-excision	DNA damage that distorts the double helix, including abnormal bases, modified bases, and pyrimidine dimers



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