A. Mutational Damage:
1. Introduction
   - Mutation rate =
   - Many
2. Classifying repair systems
   - Based on
   - Types of repairs
     a. Direct reversal
        - Reverses
     b. Replacement
        - Involves
        i. Base excision repair
        ii. Nucleotide excision
        iii. Mismatch repair
        - bases
     c. Recombination repair
        - Retrieval
        - Used
     d. Non-homologous end joining
        - Rejoins
     e. Resynthesis of
3. Classifying damages
   a. Single-base changes
      - Affect sequence of DNA,
      - Do not
      - Happens because one base is

      - Caused by:
        i. Mutation of one
        ii. Replication errors
      - Exert their effects

- Examples of single base changes
  i. Deamination
     - can occur
ii. Replication errors:
- can cause a distortion persists
- if repaired =
- if not repaired =

b. Structural distortions
- May provide
  - Introduction of covalent bond
i. Thymine (pyrimidine) dimers
ii. Addition of bulky adducts
- attachment

B. Repair Systems in Prokaryotes:
  1. Excision repair
     - Triggered by

        a. Stages of excision repair
           i. Incision
              - damaged structure

              - DNA strand

           ii. Excision
              - 5’-3’ exonuclease
iii. Synthesis
- single-stranded region serves
- new-strand synthesis

iv. Ligation of nicks
- DNA ligase

b. Enzymes of excision repair
- Most excision repair
  - *uvrA,B,C*
  - How Uvr complex works:
    i. UvrAB recognizes
    ii. UvrA dissociates;
    iii. UrvBC makes
      - 7 bases
      - 3-4 bases
    iv. UrvD (helicase) unwinds
- DNA pol I excises
- DNA pol II and DNA pol III can
- Other accessory proteins can
  - When
  - Mfd protein

2. Base flipping
   a. General considerations
      - Occurs when

      - Enzymes involved
      i. Glycosylases
         - Cleaves

      ii. Lyases
         - Opens
   b. Mechanism:
      i. Modified base
         - happens when
           • uracil found
- also occurs when

- A single human alkyladenine DNA glycosylase (AAG)

  ii. After removal of base,

  iii. DNA pol

  iv. Nick
3. Error-prone repair
   - Many repair systems are very faithful =
     - Exception is
     - Last ditch effort to
     - Places any
     - Repair system encoded by
       - Complex =
       - UmuD′₂C is a DNA polymerase V
     - Can save
     - Comes at consequence =

4. Mismatch repair
   - A mutated DNA base
     - When normal base is
     - Precautions are taken
     - System responsible
     - Major type of damage occurs
     - 8-oxo-dGTP can be
     - Incorporated O=G
a. Components of mismatch repair
   i. MutT hydrolyzes
   ii. MutM =
   iii. MutY =

   - MutM and MutY are

b. Mismatch repair and replication
   - Recall that newly replicated DNA is
     
     \[
     \begin{align*}
     & \text{GA*TC/GA*TC} \\
     & \text{GA*TC/GATC}
     \end{align*}
     \]
- DNA bases are
- Occurs faithfully
- Components of mismatch replication repair
  i. MutS binds to mismatch =
     - 1st
     - 2nd
  - creates a loop of DNA
  ii. MutL binds MutS =
  iii. MutH endonuclease
     - site is cleaved
  iv. New DNA strand
c. Mismatch repair of slippages
   - Homologues of
   - Repair mismatches that
   - Slippage occurs in region with DNA pol slips
   - Daughter strand has
   - Loop recognized

5. Recombination repair
   - Use activities that
   - Function
   - Major role is
   - Occurs when DNA pol

   a. Stages:
      i. DNA pol III
      ii. Since it cannot get past the roadblock,

      • one duplex =
      • other duplex =
iii. Piece of single-stranded DNA is

iv. The subsequent gap from the normal duplex

b. Pathways for recombination repair in *E. coli*
   i. RecBC =
   ii. RecF =
      - Both require
      - RecA can
c. Recombination repair and correcting replication errors
   - Requires the presence of a

   - Possible outcomes
     i. Fork stops moving forward;

     ii. Fork effectively
     iii. New daughter strands
     iv. Repair
     v. Helicase rolls
     vi. Replication

- Repair system
- RecA may
- RecBC involved
C. Repair Systems in Eukaryotes:
   1. Conserved elements
      a. Yeast
         - The best
         - Can identify repair systems
         - Find homologues
            a. RAD3 group =
            b. RAD6 group =
            c. RAD52 group =
            - Interesting correlation between gene expression and repair =

b. Mammals
   - Are human diseases
   - Best example =
   - Individuals can be
   - All involved
   - All have
2. Repairing double-stranded breaks
   - Double-stranded breaks
     - Can occur after
     - Are repaired by
     - Steps of NHEJ
       a. Broken end recognition
         - Heterodimer of
           - Form scaffold that
           - Recruit other enzymes =

   - crystal structure suggest that
     - each heterodimer bring
     - ligase binds
b. Filling in the ends =

c. Joining of ends