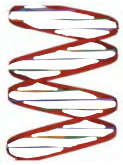
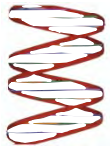
DNA Damage and Repair

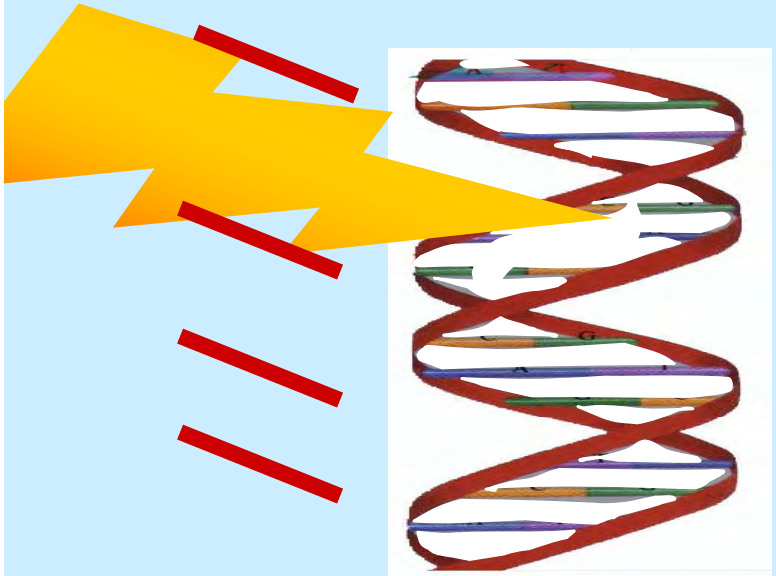
 =  ???

It is well-known that DNA can be damaged by radiation. However, DNA is routinely damaged by oxidative stress of normal cellular processes every day.

Scientists are trying to determine whether DNA damage from radiation is the same or different from normal damage.

Similarly, it is important to learn if radiation-damaged DNA is restored by the same repair mechanisms used by normally damaged DNA.

Investigation is being done to determine if the signals sent by cells with radiation-damaged DNA are different than those sent by normally damaged DNA.



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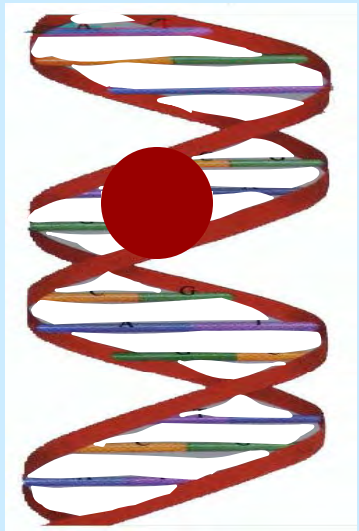


DNA Damage

There are qualitative and quantitative differences in initial DNA damage caused by radiation

- DNA damage caused by radiation exhibits multiply damaged sites and clustered legions
- Double strand breaks are more common in radiation-induced damage than single strand breaks, which are more common in normal endogenous DNA damage.

DNA Repair

- A single double strand break in DNA is easier and faster to repair than multiple damaged sites.
- Single strand break repair is usually error free.
- Double strand breaks can be either error free or error prone, containing a high error rate.

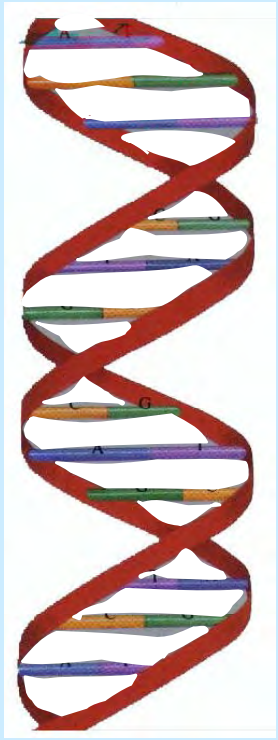
Mechanisms of Repair

- Understanding how radiation damages DNA may make it possible to identify DNA damage that is uniquely caused by radiation exposure.
- Understanding mechanisms of normal DNA repair will enable possible intervention.

Radiation can sometimes stimulate the repair of DNA

Sometime radiation may hinder the repair of DNA

Impact of Genomics on Human Risk Assessment



CTAAGG
CCATAC
TAGTCA
CATTAG
TAATTT

Identification of sequence polymorphisms

Susceptibility to toxicant and exposure

Gene expression microarrays

Mechanism of toxicity

RISK ASSESSMENT

DNA

Primary sequence

Applications

RO McClellen, CIIT

DNA Damage and Repair

- The ability for cells to repair themselves after radiation-induced DNA damage may support a threshold, or amount of radiation below which no permanent damage is done.
- Unique radiation-induced DNA damage may not be repaired easily, and could support the Linear no threshold hypothesis which says any amount of radiation can cause permanent damage.
- Radiation-induced DNA damage must be specifically linked to a disease before it can be assumed that radiation damage increases health risks from that disease. For example, damage that can be completely repaired does not necessarily equate with cancer.
- Understanding the mechanisms of DNA damage and repair will help more accurately determine risk from different levels of radiation.

DNA Damage and Repair

- Identify Damage
  - Where is it?
  - How serious is it?
- DNA Repair
  - Does it occur?
  - How much can be repaired?
  - How is it repaired?