Mistakes Happen...

MUTATION = permanent change in genetic material (nucleotide sequence)
**Mutation = change to DNA**

*Caused by:*
- errors in DNA Replication (1 in $10^9$ mistakes)
- Chemical abuse (metabolic and environmental) - mutagens
- other environmental abuse such as UV rays, ionizing radiation
If uncorrected, these changes are propagated by DNA replication.

ex.: consequences of deamination of C $\rightarrow$ U
If uncorrected, these changes are propagated by DNA replication

ex.: consequences of deamination of C $\rightarrow$ U
If uncorrected, these changes are propagated by DNA replication

ex.: consequences of Base loss
If uncorrected, these changes are propagated by DNA replication.

ex.: consequences of Base loss
Effect of single nucleotide change in DNA (= “point mutation”):

<table>
<thead>
<tr>
<th>Template strand of DNA</th>
<th>mRNA</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAC CGA TTC TTC CAA ATA CGG</td>
<td>AUG GCU AAG AAG GUU UAU GCC</td>
<td>met--ala--lys---lys---val--tyr---ala</td>
</tr>
</tbody>
</table>

**Base Substitutions**

- **Silent mutation**
  - Template strand of DNA: TAC CGA TTC TTC CAA ATA CGG
  - mRNA: AUG GCU AAG AAG GUU UAU GCC
  - Protein: met--ala--lys---lys---val--tyr---ala

- **Missense mutation**
  - Template strand of DNA: TAC CGA TTC TTG CAA ATA CGG
  - mRNA: AUG GCU AAG AAG GUU UAU GCC
  - Protein: met--ala--lys---lys---val--tyr---ala

- **Nonsense mutation**
  - Template strand of DNA: TAC CGA TTC ATC CAA ATA CGG
  - mRNA: AUG GCU AAG UAG GUU UAU GCC
  - Protein: met--ala--lys---stop
Frame Shift Mutations

Deletion

TAC CGA TTC TTC CAA ATA CGG
UAG GCU AAG AAG GUU UAU GCC
met----ala----lys----lys----val----tyr----ala

TAC CGA TTC TCC AAA TAC GGA
UAG GCU AAG AGG UUU AUG CCU
met----ala----lys----lys----phe----met----pro

Insertion

TAC CGA TTC TTT CCA AAT ACG
UAG GCU AAG AAA GGU UUA UGC
met----ala----lys----lys----gly----leu----cys
Mutations also occur in non-coding DNA sequences (only 1.5% of human genome is “coding sequences” (specifies a.a.).
(A) Human chromosome 22—48 × 10^6 nucleotide pairs of DNA

heterochromatin

10% of chromosome arm ~40 genes

1% of chromosome containing 4 genes

one gene of 3.4 × 10^4 np

regulatory DNA sequences exon intron
gene expression protein folded protein

Figure 9-25 Essential Cell Biology, 2/e. (© 2004 Garland Science)