Mutations and Cancer
Mutations and Cancer

DNA repair prevents both mutations and cancer.

Chemicals that cause cancer also cause mutations.

Cancer genes have mutations compared to their normal counterparts.

Cancer cells show a small number of mutational patterns.

Cancer cells have mutations in growth control genes.

Cancer cells have mutations in genes that are protective.

Cancer cells accumulate mutations to become more virulent.
Mutations and Cancer

-T-C-
-Å-G-
Mutations and Cancer

- UV light
- [6-4] Mutation
Mutations and Cancer

UV light → [6-4] → Replication → Mutation
Mutations and Cancer

UV light \rightarrow [6-4] \rightarrow \text{Replication} \rightarrow \text{Mutation}

DNA Repair

\text{-T-C-} \rightarrow \text{-T-T-} \rightarrow \text{-T-A-}
Mutations and Cancer

![Diagram showing the process of mutations and cancer]

- UV light
- [6-4]
- Replication
- Mutation
- DNA Repair
- Cancer
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Cancer causing agents = Mutation causing agents
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Dominant UV light mutation

$TC \rightarrow TT$

Dominant mutation in skin cancer

$TC \rightarrow TT$
Mutations and Cancer

Transfection of DNA provides a strategy for detecting non-viral oncogenes.

- Human bladder carcinoma cells
- DNA
- DNA prepared for transfection into cells
- DNA into normal mouse fibroblasts
- Morphologically transformed cell
- Transformed cells injected into mouse
- Tumor caused by RAS gene with G→T mutation
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7,042 human tumors analyzed

4,938,362 mutations analyzed

ONLY

21 mutational “Signature Patterns”

UV light = Signature 7
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Growth factors

RTK

Y-P

Y-P

RAS-GDP

RAS-GTP

RAF

RAF

MEK

ERK

Other effectors: for example, PI3K, RALGDS, PLCs

Nuclear translocation and gene expression
Mutations and Cancer

Growth factors

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![Chemical structure of PLX 4032 (Vemurafenib)](image)

**Table**

<table>
<thead>
<tr>
<th>PLX 4032</th>
<th>Vemurafenib</th>
</tr>
</thead>
</table>

This image illustrates the molecular structure of Vemurafenib, a drug used in the treatment of certain types of cancer involving mutated BRAF genes.
Mutations and Cancer

Colon Cancer Tumor Progression

<table>
<thead>
<tr>
<th>Affected event</th>
<th>Gene(s) involved</th>
<th>APC</th>
<th>KRAS</th>
<th>Smad2/4</th>
<th>p53</th>
<th>Other genetic alterations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wnt pathway activation</td>
<td>Early adenoma/Dysplastic crypt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EGFR signaling activation</td>
<td>Intermediate adenoma</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>TGFβ response inactivation</td>
<td>Late adenoma</td>
<td></td>
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<td></td>
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<tr>
<td>Loss of p53 function</td>
<td>Carcinoma</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Metastasis</td>
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<td></td>
</tr>
</tbody>
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Normal epithelium → Early adenoma/Dysplastic crypt → Intermediate adenoma → late adenoma → Carcinoma → Metastasis
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