Cancer-associated mutations affect:
- proliferation
- cell death
- angiogenesis
- cell motility
- invasion
- other

Chromosomal Abnormalities are Common in Cancer Cells

Normal

Tumor

Figure 3.7b  The Biology of Cancer (© Garland Science 2007)
In Vitro Assay for Cellular Transformation

DNA From Transformed Fibroblasts is Sufficient to Transform Recipient Cells

Clone DNA from Tumor that is Capable of Transforming Recipient Cells

Cloned Oncogene DNA Transforms but not Cloned Proto-oncogene (Normal Gene)
Sequencing Reveals Oncogene is Signaling Factor Ras!

Table 4.2 A list of point-mutated ras oncogenes carried by a variety of human tumor cells

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Proportion (%) of tumors carrying a point-mutated ras gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>90 K</td>
</tr>
<tr>
<td>Thyroid (papillary)</td>
<td>60 (H, K, N)</td>
</tr>
<tr>
<td>Thyroid (follicular)</td>
<td>55 (H, K, N)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>45 (K)</td>
</tr>
<tr>
<td>Seminoma</td>
<td>45 (K, N)</td>
</tr>
<tr>
<td>Myelodysplasia</td>
<td>40 (N, K)</td>
</tr>
<tr>
<td>Lung (non-small-cell)</td>
<td>35 (K)</td>
</tr>
<tr>
<td>Acute myelogenous leukemia</td>
<td>30 (N)</td>
</tr>
<tr>
<td>Liver</td>
<td>30 (N)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>15 (K)</td>
</tr>
<tr>
<td>Bladder</td>
<td>10 (K)</td>
</tr>
<tr>
<td>Kidney</td>
<td>10 H</td>
</tr>
</tbody>
</table>

H, K, and N refer to the human H-RAS, K-RAS, and N-RAS genes, respectively.


Signal Transduction - Slide 6 - 7.013 - 3/21/07

GROWTH/PROLIFERATION

Cell division
Normal allele of myc

Translocation Between Two Chromosomes Fuses myc proto-oncogene to New Highly Active IgH Promoter

Because we carry two copies of all genes, two mutational events are required to eliminate the function of a tumor suppressor gene.

New approaches to cancer therapy

- Targeted therapies against pathways/genes activated in cancer cells:
  - Ras therapies
  - EGF Receptor
  - Angiogenesis

- Therapies to replace lost genes:
  - gene therapy

- Cancer vaccination
  - e.g., HPV vaccines