Neoplasia II: Tumor Characteristics
Tumor Characteristics Lecture Objectives

• Define tumor differentiation, and explain the difference between well-differentiated, moderately-differentiated, and poorly-differentiated tumor cells.

• Define anaplasia, and describe what anaplastic cells typically look like.

• Define dysplasia, describe what dysplastic cells look like, and explain why it matters whether cells are mildly, moderately, or severely dysplastic.

• Explain what “growth fraction” means, and list some factors that affect a tumor’s growth fraction.

• Describe the three ways tumors metastasize.

• Compare and contrast grading and staging (just know what they are...don’t memorize tiny details!)
Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia
- Rate of growth
- Metastasis
- Grading and staging
Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia
Differentiation

Differentiation = the degree to which tumor cells resemble their cell of origin

- Well-differentiated: closely resemble
- Moderately-differentiated: sort of resemble
- Poorly-differentiated: barely resemble

Benign tumors are usually well-differentiated
Malignant tumors can show any level of differentiation
Thyroid adenoma, well-differentiated
Squamous cell carcinoma, well-differentiated
Intercellular bridges

Squamous cell carcinoma, poorly-differentiated
Anaplasia

Anaplasia = a state of complete un-differentiation

- Literally, “to grow (-plasia) backwards (ana-)”
- Means tumor cells do not resemble their cell of origin at all
- Almost always indicates malignancy
Characteristics of Anaplastic Cells

• Pleomorphism
• Hyperchromatic, large nuclei
• Bizarre nuclear shapes, distinct nucleoli
• Lots of mitoses, and atypical mitoses
• Architectural anarchy
Anaplastic carcinoma
Abnormal mitoses

Lots of mitoses
Dysplasia

Dysplasia = disorderly (dys-) growth (-plasia)

• Used to describe changes in non-neoplastic epithelial cells
• Graded as mild, moderate, or severe
• Next step after severe dysplasia is carcinoma in situ
• ...and the next step after that is invasive carcinoma
Dysplastic cells show:

• Pleomorphism
• Hyperchromatic, large nuclei
• Lots of mitoses
• Architectural anarchy
Q. Wait a minute, “dysplasia” sounds suspiciously similar to “differentiation” – what’s the difference?

A. Both terms describe whether cells look normal or not!

BUT:

Dysplasia is used to describe non-neoplastic cells, and differentiation is used to describe neoplastic cells.

Dysplasia is used to describe epithelial cells, and differentiation can be used to describe any cell type.
Dysplasia

Non-neoplastic epithelial cells

- Mild dysplasia
- Moderate dysplasia
- Severe dysplasia

Differentiation

Neoplastic cells

- Well-differentiated
- Moderately-differentiated
- Poorly-differentiated
- Anaplastic
Normal glandular epithelium

- Crowding
- Hyperchromatic nuclei

Mild dysplasia

- Architectural anarchy

Moderate dysplasia

- Pleomorphism

Severe dysplasia
Invasive carcinoma
Tumor Characteristics Lecture Outline

- Differentiation, dysplasia, and anaplasia
- Rate of growth
Generalizations about Tumor Growth

• Malignant tumors grow faster than benign ones.
• Poorly-differentiated tumors grow faster than well-differentiated ones.
• Growth is dependent on:
  • Blood supply
  • Hormonal factors
  • Emergence of aggressive sub-clones
Growth Fraction

- Growth fraction (GF) = % of tumor cells that are dividing
- Age of tumor matters
  - Early on (subclinical), GF high.
  - Later (clinically detectable), GF low.
- Type of tumor matters
  - Leukemias, lymphomas, small-cell lung cancer: high GF
  - Breast, colon cancer: low GF
- Important for treatment
  - High GF tumor: treat with chemotherapy/radiation
  - Low GF tumor: treat by debulking
Normal cell

Single tumor cell

30 doublings

1 gm – 10^9 cells
Smallest clinically detectable mass

10 doublings

1 kg – 10^{12} cells
Maximum mass compatible with life

Microscopic metastases

Metastases
Tumor Characteristics Lecture Outline

• Differentiation, dysplasia, and anaplasia
• Rate of growth
• Metastasis
Metastasis

Metastasis = development of secondary tumor implants in distant tissues

Half of all patients with malignancies have mets at the time of diagnosis!!

The speed and location of metastasis is related to:

- Type of tumor
- Size of tumor
- Degree of differentiation of tumor
Liver with multiple metastases
Three Ways Tumors Metastasize

Seeding
Lymphatic spread
Hematogenous spread
Three Ways Tumors Metastasize

Seeding

- Tumor floats through a body cavity
- Bits break off and implant on peritoneal surfaces
- Ovarian cancer can spread easily this way
Liver seeded with metastatic ovarian carcinoma
Three Ways Tumors Metastasize

Seeding

Lymphatic spread

• Tumor spreads through lymphatics
• Sentinel lymph node first
• Carcinomas prefer to spread this way
Tumor in lymphatic
Tumor in lymph node
Tumor in lymph node
Three Ways Tumors Metastasize

Seeding

Lymphatic spread

Hematogenous spread

• Tumor spreads through blood vessels
• Liver and lungs are the most common destinations
• Sarcomas prefer to spread this way
Sarcoma metastatic to lung
Neoplasia Outline

- Differentiation, dysplasia, and anaplasia
- Rate of growth
- Metastasis
- Grading and staging
Grading and Staging

• Used for malignant tumors
• Useful for determining treatment and prognosis

• Grading
  • Tells you how nasty the tumor looks
  • Use microscope
  • Can be useful in some tumors

• Staging
  • Tells you how far the tumor has spread
  • Use imaging
  • Very useful in most tumors
Grading system for breast cancer

<table>
<thead>
<tr>
<th>Tubules</th>
<th>Pleomorphism</th>
<th>Mitoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>lots of tubules</td>
<td>small, uniform cells</td>
<td>0-9 mitoses/10 hpf</td>
</tr>
<tr>
<td>some tubules</td>
<td>larger, less uniform cells</td>
<td>10-19 mitoses/10 hpf</td>
</tr>
<tr>
<td>rare tubules</td>
<td>markedly pleomorphic cells</td>
<td>≥20 mitoses/10 hpf</td>
</tr>
</tbody>
</table>

Add all points together

<table>
<thead>
<tr>
<th>Score</th>
<th>Grade</th>
<th>5y survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-5</td>
<td>Low grade</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>6-7</td>
<td>Intermediate grade</td>
<td>80%</td>
</tr>
<tr>
<td>8-9</td>
<td>High grade</td>
<td>60%</td>
</tr>
</tbody>
</table>
Breast carcinoma low grade
Breast carcinoma high grade

mitoses

pleomorphism
TNM staging system for non-small cell lung cancer

**T = Tumor size**
- Tis – in situ tumor
- T1 – small tumor
- T2 – larger tumor
- T3 – larger or invasive tumor
- T4 – very large/very invasive

**N = Nodes**
- N0 – no lymph node involvement
- N1 – a few regional nodes
- N2 – lots of regional nodes
- N3 – distant nodes

**M = Metastases**
- M0 – no metastases
- M1 – metastases
## TNM staging system for non-small cell lung cancer

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Treatment</th>
<th>5y survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>Surgery only</td>
<td>75%</td>
</tr>
<tr>
<td>Stage I</td>
<td>T1 or T2</td>
<td>N0</td>
<td>M0</td>
<td>Surgery ± radiation</td>
<td>50%</td>
</tr>
<tr>
<td>Stage II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
<td>Surgery and radiation ± chemotherapy</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>T1 or T2</td>
<td>N2</td>
<td>M0</td>
<td>Chemotherapy ± radiation to debulk</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1 or N2</td>
<td>M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
<td>Maybe surgery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>Any N</td>
<td>M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>Palliative care</td>
<td>&lt;2%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Maybe chemo or radiation</td>
<td></td>
</tr>
</tbody>
</table>