**Microinvasive carcinoma**

- “...one or more clearly separate small, microscopic foci of infiltration into non-specialized interlobular stroma”
- Variable definitions
- Levels and/or myoepithelial markers variably helpful
- If doubt exists, should be classified as in situ carcinoma

Myoepithelial cells (MECs)

- Semi-contractile cells lining breast terminal ducts and lobules
- Absence of myoepithelial layer (basement membrane) "diagnostic" of invasive cancer
### Immunophenotype

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Localization</th>
<th>Pattern</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Also reacts with</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth muscle actin</td>
<td>Membrane</td>
<td>Continuous</td>
<td>Very good</td>
<td>Good</td>
<td>Myofibroblasts, vessels</td>
</tr>
<tr>
<td>Calponin</td>
<td>Membrane</td>
<td>Continuous</td>
<td>Very good</td>
<td>Good</td>
<td>Myofibroblasts, vessels</td>
</tr>
<tr>
<td>p63</td>
<td>Nuclear</td>
<td>Discontinuous</td>
<td>Very good</td>
<td>Very good</td>
<td>Metaplastic carcinomas, subset of ductal carcinomas</td>
</tr>
<tr>
<td>Smooth muscle myosin heavy chain</td>
<td>Membrane</td>
<td>Continuous</td>
<td>Moderate</td>
<td>Good</td>
<td>Vessels</td>
</tr>
<tr>
<td>CD10</td>
<td>Membrane</td>
<td>Discontinuous</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Many cell types</td>
</tr>
<tr>
<td>HMWK</td>
<td>Membrane</td>
<td>Continuous</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Myofibroblasts, subset of carcinomas</td>
</tr>
</tbody>
</table>
MEC staining in DCIS

- 101 excisional biopsies of DCIS with and without associated invasive cancer
- 84% of cases showed reduced staining intensity of 1 or more MEC markers compared to staining in normal ducts
- 77% of cases with decreased/no expression on DCIS-associated MECs by SMMHC staining (significant by grade as well)
- No significant differences in DCIS with or without associated invasive cancer

MEC staining in DCIS

Cases with decreased/no expression in DCIS-associated MECs

<table>
<thead>
<tr>
<th>Marker</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>SMA</td>
<td>1%</td>
</tr>
<tr>
<td>p75</td>
<td>4%</td>
</tr>
<tr>
<td>p63</td>
<td>13%</td>
</tr>
<tr>
<td>Calponin</td>
<td>17%</td>
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<tr>
<td>CK5/6</td>
<td>30%</td>
</tr>
<tr>
<td>CD10</td>
<td>34%</td>
</tr>
<tr>
<td>SMMHC</td>
<td>77%</td>
</tr>
</tbody>
</table>


Challenging Breast Case

Area 1
Challenging Breast Case
Area 2
Diagnosis

GRADE 2 INVASIVE DUCTAL CARCINOMA (3 MM), ARISING IN A BACKGROUND OF MULTIFOCAL HIGH GRADE DUCTAL CARCINOMA IN SITU
Invasive carcinoma

MECs as tumor microenvironment
- Role in development
- Physical barrier
- Tumor suppressor functions
- Paracrine effects?

MECs in the tumor microenvironment
- Normal functional genes downregulated (including laminin)
- Proliferation, migration, invasion, angiogenesis genes upregulated
- Degradative enzymes increased
- DNA methylation
- Immunophenotype altered

Encapsulated papillary carcinoma (EPC)

- Collagen IV staining in 21 pure EPCs (majority showed no staining with p63 or SMMHC)
- Collagen IV staining not seen in 6 IDCs (also lacked MEC markers)
- 1 patient with micrometastasis at mean follow-up of 40 months


What does it all mean?

- Tumor-MEC and tumor-stroma interactions appear meaningful and relatively reproducible in the research literature
- MEC and stromal cells may be potential pharmaceutical targets
- Different MEC (or other cell) markers may be discovered
- Much more research needed

Practical Points

- Microinvasion is very rare
- Describe the criteria used for microinvasion; measure largest focus and provide number of foci if > 1
- Adequately fix tissue
- Routinely use more than 1 MEC marker; consider adding more as needed
- Examine sections for strong internal control

References