Review and Updates of Immunohistochemistry in Selected Salivary Gland and Head and Neck Tumors
- Monophasic tumors: myoepithelioma, acinic cell carcinoma, and salivary duct carcinoma.

- Biphasic tumors includes tumors pleomorphic adenoma, epithelial-myoeplithelial carcinoma, and adenoid cystic carcinoma.

- Some tumors demonstrate other unique cellular differentiation, such as sebaceous adenoma/carcinoma, Warthin’s, and mucoepidermoid carcinoma.
The acinar/ductal epithelial cells are:

- Positive for keratins (CK7 and CAM 5.2) and epithelial membrane antigen (EMA).
- They are focally positive or negative for high molecular-weight keratins (HMWKs; CK5/6)
- Negative for p63, myoid markers (smooth muscle myosin heavy chain, smooth muscle actin, calponin), and CK20
Myoepithelial cells:

- Positive for p63, myoid markers, vimentin, S100, and HMWKs (CK5/6),
- Weak expression for CK7 and CAM 5.2
- No expression for EMA.
Basal cells:
• Positive for p63 and HMWKs (CK5/6, 34bE12)
• Weakly positive or negative for CK7, CAM 5.2 and myoid markers (SMA, calponin)
• Negative for CK20, vimentin, S100, and EMA.

• (p63 also stains squamous epithelium)
SOX10 expression (Myoepithelial cells, Schwann cells, melanocytes)

- SOX10-positive tumors
  - Acinic cell carcinomas
  - Adenoid cystic carcinomas
  - Epithelial-myoeipithelial carcinomas
  - Myoepithelial carcinomas
  - Pleomorphic adenomas

- SOX10-negative tumors
  - Salivary duct carcinomas
  - Mucoepidermoid carcinomas
  - Squamous cell carcinomas
  - Oncocytic carcinomas/oncocytomas
Acinic Cell Carcinoma
Acinic Cell Carcinoma

- Demonstrates both serous acinar and intercalated ductal epithelial differentiation.

- Express CK7 and CAM 5.2

- Negative for p63 and CK20, myoid markers.

- Positive for DOG1.

  (DOG1 with PAS can be used to distinguish it from mammary analogue secretory carcinoma)
Mammary Analogue Secretory Carcinoma

- Histologically, immunohistochemically, and genetically similar to secretory carcinoma of the breast.
- The tumor has a t(12;15)(p13;q25) ETV6-NTRK3 translocation that is also present in breast secretory carcinoma.
Mammary Analogue Secretory Carcinoma
• Positive for S100, mammaglobin, CK7, CK19, 34bE12, EMA, MUC1, MUC4, and vimentin.
• Basal cell/myoepithelial cell markers usually do not show expression in the tumor.

• Negative for ER, PR, androgen receptor, HER2/neu

• The MIB-1 indices range between 5% and 28%.

• Recurrent $ETV6$-$NTRK3$ translocation.
## ACINIC CELL vs. MAS CARCINOMA

<table>
<thead>
<tr>
<th>Marker</th>
<th>Acinic cell carcinoma</th>
<th>Mammary analogue secretory carcinoma</th>
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</thead>
<tbody>
<tr>
<td>CK8, CK 19</td>
<td>NEGATIVE</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>GCDFP-15, Mammoglonin</td>
<td>RARELY POSITIVE</td>
<td>POSITIVE</td>
</tr>
<tr>
<td>MUC4, S100</td>
<td>NEGATIVE</td>
<td>POSITIVE</td>
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</table>
• mammaglobin and S100 expression can be seen in polymorphous low-grade adenocarcinomas (60%) and adenoid cystic carcinomas (13.3%).

• However both these tumors are positive for p63 and negative for GCDFP-15.
Mucoepidermoid carcinoma
Mucoepidermoid carcinoma

- Positive for CK5, CK6, CK7, CK8, CK14, CK18, CK19, EMA, CEA, and p63

- CK20, SMA, muscle specific actin (MSA), and S100.
Mucoepidermoid carcinoma

- Strong staining for p63 helps differentiating Mucoepidermoid carcinoma from acinic cell carcinoma, oncocytoma and oncocytic carcinoma and mammary analogue secretory carcinoma.
Myoepithelial Carcinoma

- Immunoreactivity for both keratins and at least 1 myoepithelial marker is required for the diagnosis.

- vimentin, calponin, S100, CK AE1/3, 34bE12, CAM 5.2, EMA caldesmon, SMA, MSA, GAFP

- Calponin is the most sensitive and specific marker to identify myoepithelial differentiation.

- A panel including CK AE1/3, CAM 5.2, CK5/6, calponin, SMA, S100, and vimentin, can be helpful to make an accurate diagnosis.
# Markers for Salivary Gland Tumors With Clear Cell Differentiation

<table>
<thead>
<tr>
<th></th>
<th>ACC</th>
<th>MEC</th>
<th>MC</th>
<th>EMC</th>
<th>OC/OCA</th>
<th>CCC</th>
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</thead>
<tbody>
<tr>
<td>p63</td>
<td>_</td>
<td>+</td>
<td>+</td>
<td>+ outer</td>
<td>Scant peripheral</td>
<td>+</td>
</tr>
<tr>
<td>Calponin/SMA/SM</td>
<td>_</td>
<td>_</td>
<td>+</td>
<td>+ outer</td>
<td></td>
<td>_</td>
</tr>
<tr>
<td>MHC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CK7/CAM 5.2</td>
<td>+</td>
<td>_</td>
<td>+/-</td>
<td>+ inner</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>SOX10</td>
<td>+</td>
<td>_</td>
<td>+</td>
<td>+</td>
<td></td>
<td>_</td>
</tr>
</tbody>
</table>
Salivary Duct Carcinoma
• AR, GCDFP-15, GATA3, CK AE1/3, CK7, 34bE12, CEA, and EMA.

• Ki-67 expression markedly increased.

• The immunophenotype AR+/ER-/PR-/GCDFP+ is characteristic of salivary duct carcinoma, but it does not completely exclude metastasis from the breast, which might also be AR+, ER/PR –

• 80% of salivary duct carcinomas show HER2/ neu and p53 overexpression, which correlates to poor prognosis.
• Prostatic acid phosphatase and prostate-specific antigen expression can be detected.
• In men with unknown prostatic acid phosphatase–positive and prostate-specific antigen positive metastatic carcinoma, salivary duct carcinoma should be included in the differential diagnosis in addition to prostatic adenocarcinoma.
• CK7 and HMWKs are helpful.
## Markers for Salivary Gland Tumors With Oncocytic Differentiation

<table>
<thead>
<tr>
<th></th>
<th>MEC</th>
<th>EMC</th>
<th>ACC</th>
<th>OC/OCA</th>
<th>SDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>p63</td>
<td>+</td>
<td>+outer layer</td>
<td>_</td>
<td>+ peripheral</td>
<td>_</td>
</tr>
<tr>
<td>Calponin/SMA/SMMHC</td>
<td>_</td>
<td>+outer layer</td>
<td>_</td>
<td>_</td>
<td>_</td>
</tr>
<tr>
<td>CK7/CAM5.2</td>
<td>_</td>
<td>+ inner layer</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>AR</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>+</td>
</tr>
<tr>
<td>SOX10</td>
<td>_</td>
<td>+</td>
<td>+</td>
<td>_</td>
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Adenoid Cystic Carcinoma

A delicate cribriform pattern with pseudocysts

Adenoid cystic carcinoma
Adenoid Cystic Carcinoma

- Malignant biphasic epithelial tumor composed of modified myoepithelial and ductal cells.
- Both ductal and myoepithelial/basal cell markers, such as CK7, CAM 5.2, calponin, SMA, SMMHC, p63, SOX10, and S100.
- Most adenoid cystic carcinomas showed strong and diffuse expression of c-KIT
Adenoid Cystic Carcinoma

- Overexpression of Ki-67 and p5 associated with poor prognosis.
- A recurrent t(6;9)(q22-23;p23-24) translocation identified in adenoid cystic carcinoma. This leads to the fusion of MYB and NFIB.
Differentiation of Adenoid Cystic Carcinoma, Polymorphous Low-Grade Adenocarcinoma, and Pleomorphic Adenoma

<table>
<thead>
<tr>
<th></th>
<th>c-KIT</th>
<th>Calponin/SMA</th>
<th>CK7</th>
<th>MIB-1</th>
<th>PLGA1</th>
<th>GFAP</th>
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<tbody>
<tr>
<td>PA</td>
<td>-/+</td>
<td>+</td>
<td>+ luminal</td>
<td>&lt;5%</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>PLGA</td>
<td>-/+</td>
<td>-</td>
<td>+ all cells</td>
<td>&lt;5%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>AdCC</td>
<td>+</td>
<td>+</td>
<td>&gt; 10% luminal cells</td>
<td>-</td>
<td>-</td>
<td>-</td>
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