Salivary Gland FNA
“ATYPICAL”: Criteria and Controversies

W.C. Faquin, M.D., Ph.D.
Director, Head and Neck Pathology
Massachusetts General Hospital
Massachusetts Eye and Ear Infirmary
Harvard Medical School
Boston, MA USA
A 45 yo man with a 6 month history of an enlarging left parotid gland mass.
Case:
A CT scan revealed a 3.7 cm mass in the superficial lobe of the left parotid gland. An FNA was performed.
What is your FNA Diagnosis?
CASE

CYTOLOGIC DIAGNOSIS:
NEOPLASTIC:
UNCERTAIN MALIGNANT POTENTIAL
Basaloid neoplasm with mild atypia. See note.
Note: The differential diagnosis includes basal cell adenoma and other basaloid salivary gland tumors.
CASE

SURGICAL RESECTION:
Superficial parotidectomy was performed. A frozen section performed at the time of surgery favored a basal cell adenoma.
CASE

HISTOLOGIC DIAGNOSIS: BASAL CELL ADENOCARCINOMA, 3.7 CM, SOLID TYPE.

Clinical follow-up: The patient has been free of disease for 10 years.
BASAL CELL ADENOCARCINOMA

- Low-grade salivary gland neoplasm
  - 2% of malignant salivary gland tumors
  - Malignant counterpart of basal cell adenoma
  - Parotid gland, rarely in submandibular gland
  - Average age: 60 years (range: 27-92 years)

- Good prognosis:
  - Local recurrence (35%), infrequent metastatic disease (10%), and low mortality (3%)

- Complete surgical excision with disease-free margins
Basal Cell Adenoma & Adenocarcinoma

**Immunohistochemistry:**
- Positive for keratin 7, CEA, EMA
- Positive for myoepithelial markers
- **Nuclear beta-catenin** +
Basal Cell Adenoma & Adenocarcinoma

- CTNNB1 mutation – 3p21
- Beta-Catenin overexpression
  - Present at cell junctions
  - Part of WNT signaling pathway
Nuclear Beta-Catenin in Basal Cell Adenoma

The Key DDX for Basaloid Neoplasms:
Basal Cell Adenoma/Adenocarcinoma
Adenoid Cystic Carcinoma
Cellular Pleomorphic Adenoma
Proposed Classification Scheme

1) Non-Diagnostic
2) Non-Neoplastic
3) Atypia of undetermined significance
4) Neoplastic:
   - a) Benign
   - b) Uncertain malignant potential
5) Suspicious for Malignancy
6) Malignant
With an expanded array of IHC and new molecular advances, FNA and small biopsies are becoming more effective.
### Increasing Availability of Molecular Markers For Salivary Gland Tumors

- **Mammary analogue secretory carcinoma:**
  - ETV6-NKRT; t(12:15)

- **Pleomorphic adenoma & Ca ex PA:**
  - PLAG1; t(3;8)
  - HMGA2 rearrangement

- **Clear cell carcinoma:**
  - EWSR1-ATF1; t(12:22)

- **Mucoepidermoid carcinoma:**
  - MECT1/MAML2; t(11:19)

- **Cribriform Adenocarcinoma:**
  - PRKD rearrangement

- **Adenoid cystic carcinoma:**
  - MYB-NFIB; t(6:9)

- **Basal Cell Adenoma**
  - CTNNB1 mutations
Most Pleomorphic Adenomas Are Accurately Diagnosed by FNA
Cellular Pleomorphic Adenoma:
Can be difficult to distinguish from other basaloid neoplasms
Pleomorphic Adenoma

**Immunohistochemistry:**
- Positive for keratin 7, CEA, EMA
- Positive for myoepithelial markers
- PLAG1 +
Pleomorphic Adenoma

Cytogenetics:

- **PLAG1 rearrangements (50-60%)**
  - Present in PAs in different tissues
  - Nuclear localization
  - Functions to activate transcription (Zn finger)

- **HMGA2 rearrangements (10%)**
PLAG-1 Immunoreactivity: Overexpressed in 94% of PA

Contributed by Dr. J. Krane, BWH
Adenoid Cystic Carcinoma:
Classic Cribriform Pattern often Recognizable by FNA
Solid Adenoid Cystic Carcinoma: Difficult to diagnose by FNA
Adenoid Cystic Carcinoma

**Immunohistochemistry:**
- Positive for keratin 7, CEA, EMA
- Positive for myoepithelial markers
- CD117 (KIT) +
- MYB +
Immunoreactivity for CD117 (KIT) in AdCC

Luminal Cells +
Adenoid Cystic Carcinoma: Recent Advance – MYB Translocation

**Cytogenetics:**

- t(6:9) MYB oncogene-NFIB transcription factor
- In salivary gland, this finding by FISH is specific for AdCC

FISH contributed by Dr. Joaquin Garcia, Mayo Clinic
MYB immunostaining is a useful ancillary test for distinguishing adenoid cystic carcinoma from pleomorphic adenoma in FNAB specimens.
# A Challenging DDX in the Salivary Gland: PA vs AdCC vs BCA

<table>
<thead>
<tr>
<th>PA</th>
<th>AdCC</th>
<th>BCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chondromyxoid/ embedded cells</td>
<td>• Matrix spheres acellular</td>
<td>• Peripheral matrix ribbons</td>
</tr>
<tr>
<td>• PLAG1+, GFAP +</td>
<td>• MYB+, CD117+</td>
<td>• Nuclear b-catenin+</td>
</tr>
<tr>
<td>• Myoep predominant</td>
<td>• Small basaloid cells</td>
<td>• 2 basaloid cell populations</td>
</tr>
</tbody>
</table>

- **PA**: Chondromyxoid/embedded cells, PLAG1+, GFAP+, Myoep predominant
- **AdCC**: Matrix spheres acellular, MYB+, CD117+, Small basaloid cells
- **BCA**: Peripheral matrix ribbons, Nuclear b-catenin+, 2 basaloid cell populations
Key Points

• FNA of basaloid neoplasms may be the single most difficult diagnostic problem in the salivary gland
• Milan System: Neoplastic - UMP
• A descriptive diagnosis and DDX is often used
• New immunohistochemical and molecular markers may increase the accuracy of FNA for basaloid tumors
Thank You!