BEST PRACTICES IN THE APPLICATION OF IMMUNOHISTOCHEMISTRY TO DIAGNOSTIC UROLOGIC PATHOLOGY: LESSONS FROM USES & ABUSES

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Best “Special Studies” in Surgical Pathology

- Good thin section and well stained H&E slides
- Additional sections, recuts and levels
- A phone call to the clinician (or reviewing the electronic medical records)
- Another trust-worthy pair of eyes (colleague)
- Placing the diagnostic dilemma in context of the clinical situation and management considerations
- Having a best practice approach Immunohistochemistry

Toward Best Practice IHC use in routine practice

- When IHC stains exceed H&E stain
  - complex case OR
  - Lack of best practice approach
**Toward Best Practice IHC use in routine practice**

- Foundation is the integration of clinical history, gross examination & microscopy
- Cornerstone is still the H&E with appropriate and judicious IHC support – *IHC guides and does not dictate the diagnosis*
- Practice made considerably more objective by ancillary techniques e.g. IHC

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**Toward Best Practice IHC use in routine practice**

- Serious misdiagnoses are made by inappropriate use of IHC or incomplete knowledge of antibody/ies
  - More is not necessarily better
  - IHC adjunctive method, histology key
    - *If you have no idea, don’t mark it*
- Start with a question based on morphology
- Apply a judiciously constructed panel based on the differential diagnosis generated by the case

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**Toward Best Practice IHC use in routine practice**

- Panel should include expected positive and expected negatives
- There are no absolutely specific or sensitive antibodies
  - Anomalous stuff happens
  - Sensitivity and specificity is not inherent to the antibody, but to the antibody applied in a given setting
- Evaluate the stain paying attention to pattern (*nuclear, cytoplasmic, membranous, etc.*)
- ALWAYS evaluate the controls (*positive and negative*)
- Diagnose the case after review of IHC only in the context of the morphology and the clinical situation
GOWN’S LAWS OF IMMUNOCYTOCHEMISTRY

- There is no perfect marker of any tumor
- There is no perfect fixative for all antibodies
- If everything in the tissue section appears positive, nothing is actually positive
- All that turns brown (or black, or red, etc.) on the slide is not positive
- Under inappropriate conditions, any antibody can be made to appear positive on any tissue
- In any given immunocytochemical run involving multiple slides, tissue will fall off the slide corresponding to the most critical antibody
- The diagnostic power of any immunocytochemical preparation is no greater than the knowledge and wisdom of the pathologist interpreting it

SELECT BEST PRACTICE IHC APPLICATIONS IN UROLOGIC PATHOLOGY

- **Bladder:**
  - Proving origin/differentiation in unusual primary or at a metastatic site
  - IHC in flat intraepithelial lesions
- **Prostate:**
  - Proving origin at a metastatic site
- **Kidney:**
  - Proving renal origin at a metastatic site
- **Testis:**
  - Screening panels for tumors involving testis – primary or metastatic sites
  - Characterizing the various germ cell components

PROVING UROTHELIAL DIFFERENTIATION

| Carcinoma of unknown origin or patient with history of bladder cancer: |
| Lymph node | Lung | Liver | Bone | Prostate |
| Metastatic tumors to the bladder: |
| Melanoma | Prostate | Colorectal | Cervix | Ovary | Renal |
| Primary urothelial carcinoma: |
| UCa with small tubules | Plasmacytoid | MICropapillary | Etc |
CA in a cervical LN

CA in the bladder, h.o of lung cancer

UROTHELIAL CARCINOMA
(Prim. or Metastatic site)

Challenges:
- Poorly differentiated carcinoma
- “Characterless”: solid, nested & trabecular architecture

Hallmarks:
- Frequent squamous and / or glandular diff.
- Cells with nuclear grooves
- Nuclear atypia obvious +/- anaplasia

Approach
- Clinical history (invasive, usually high stage carcinoma)
- Compare with primary
- Judicious IHC: ? Best markers
Paraganglioma

Epith. LMS

PEComa

Melanoma

**URINARY BLADDER - IHC**

*Diagnosis of metastatic urothelial cancer*

- **CK7 (+) (>90%)**
- **CK20 (+) (40-70%)**
- **p63 (+) (60-90%)**
- **High molecular weight cytokeratin 34βE12 (+) (60-90%)**
- **GATA3 (60-70%)**
- **Uroplakin II (+) (50-80%)**
- **S100P (70-80%)**
- **Uroplakin III (+) (20-50%)**
- **Thrombomodulin (+) (60-75%)**
- **CEA, Leu-M1 (+) (minimal value)**
Plasmacytoid U Ca

Plasmacytoid U.Ca - CK20

GATA 3 & S100P

• Markers of urothelium and urothelial carcinoma by cDNA microarray

S100P (commercial)

- Nuclear staining accompanied by cytoplasmic staining
- More sensitive but less specific than GATA3
- Other tumors stained: pancreaticobiliary, breast?

GATA3

- Nuclear staining
- Lower sensitivity but higher specificity than S100P for urothelium
GATA3 – Wide Range of Expression

- Positive in
  - Breast, trophoblastic tumors, paragangliomas, salivary gland neoplasms, squamous carcinomas, basal cell carcinomas, yolk sac tumors, pancreatic ductal adenocarcinomas

Uroplakins – II and III

- Protein constituents of the urothelial plaques in vesicles of urothelium
- Vital role in expansion and contraction through vesicle cycling
- Subunits uroplakins Ia, Ib, II, and IIIa
- Unique and characteristic feature of urothelium
- Previous data for UP3, new data for UP2

Uroplakin 2 versus Uroplakin 3

Among UC metastases, UP2 showed greater intensity and proportion, (both p<0.001), with higher sensitivity (73% vs 37%, respectively, p=0.001).

Smith et al. Histopathology, in press.
Uroplakin 2 versus Uroplakin 3

Villoglandular variant simulates colorectal carcinoma

Smith et al. Histopathology, in press
IMMUNOHISTOCHEMISTRY IN FLAT LESIONS OF THE BLADDER

Panel: p53, CD44 (standard isoform), CK20

Indications:
- Marked denudation – residual basal cells vs “clinging” CIS
- Distinction between reactive atypia and CIS (large cell non-palaeomorphic or “small” cell)
- Pathologist favors CIS but has reservations making diagnosis
- CIS with unusual morphology – Pagetoid, undermining, etc.

Caveats:
- Not applicable for dysplasia vs CIS
- Greater caution while evaluating post-treatment biopsies
Reactive

CD44

Reactive - CK20

Reactive - p53

CA-INSITU
p53: 55-80% of CIS

CK-20 (+): 50-100% of CIS

CD44 (-): 96-100% of CIS
Regenerative basal cells vs. clinging CIS

CK20 (+)
CD44(-)
**UROTHELIAL ASSOCIATED-MARKERS**

Prostate vs. Urothelial Carcinoma
- Often in bladder neck specimens
- Therapeutically critical differential

- CK20
- P63 or MWCK
- PSA
- PSAP
- NKX1.3
- Prostein (P501S)
- ERG-TMPRSS2
- PSMA

**CAUTION:** Both may coexist!

**New Prostate Lineage Associated Markers**

Prostein (P501S): Granular Golgi Pattern
- Prostatic carcinoma independent of Gleason pattern and metastatic status
- Rarely in villous adenoma and adenocarcinoma of bladder

NKX3.1: Nuclear Pattern
- Prostatic epithelium, testis, bronchial mucous glands, rare urethral urothelial cells
- Prostatic carcinoma and infiltrating lobular carcinoma

Prostate Specific Membrane Antigen (PSMA): Membranous
- Prostatic epithelium, endometrial glands, duodenal mucosa, proximal renal tubules, urothelium, neuroendocrine cells of colonic crypts and endothelium
- Prostatic adenocarcinoma, gastric carcinoma, small cell carcinoma of lung, urothelial carcinoma and GBM
Atypical focus

Mimics of malignancy:
- Atrophy
- Basal hyperplasia
- etc.

Non prostatic origin
- Prostatic origin
- Mesonephric remnants
- Cowper glands
- PIN

Architecture
- Basal layer
- Nuclear features
- Quantity
- Additional morphologic features
- IHC

To confirm focus as cancer
- Confirm benignity in ASAP felt to be benign
- Unusual patterns
  - Atrophic
  - Pseudohyperplastic
  - Double – layer
  - PIN-like

Indications for IHC – Needle Biopsy

Atypical small cell proliferations
- Atypical large acinar proliferations (intraductal patterns)
- Post – treatment setting
**IHC in a pt. with one (+) core**

- **Confirm bilaterality** - clinical staging - almost 50% patients with prostate cancer treated with RT
- **Accurate assessment of # of cores involved** – Active surveillance
- **Quantitation of cancer** – Active surveillance (>50% may exclude)

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**Quantitation of Tumor Involvement**

![Image showing quantitation of tumor involvement]

- eyeball estimate: 10%
- linear measurement: 4 mm
- % of core involvement: 4 mm / 20 mm = 20%

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**Work-up of Atypical Foci with Definite Cancer in Other Parts**

Patient with Gleason score 3+4 or higher grade cancer on at least one part.

? Work up other parts with small foci of possible 3+3=6

Generally, not indicated, as additional IHC confirmation will likely not change management.
IHC in Prostate Needle Bxs.

- **Basal cell cocktail**
  - p63 and 34βE12
- **Triple cocktail “PIN cocktail”**
  - p63/34βE12/AMACR
- **ERG immunohistochemistry**
  - Additional marker, only if triple not conclusive

PSA – to prove prostate origin – NA, Cowper’s glands

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**Triple cocktail**

- HWCK/p63 (CK5/6) – basal cells
- AMACR – cancer cells
- 37 – 68% of “atypical” cases were confirmed as cancer
- Overcomes problems associated with individual markers
- Foci often limited
Review with respect to external & titration of antibody is very important internal controls

**Triple cocktail**

- **Expected reactions**
  - **PCa:** p63(-), HMCK(-), AMACR(+)
  - **Benign small cancer mimics:** p63, HMCK(+), AMACR(-)
  - **HGPIN:** p63, HMCK(+), AMACR(-/+)
- **Ductal cancer:**
  - **Invasive component:** p63, HMCK(-), AMACR(+)
  - **Intraductal component:** p63, HMCK(+), AMACR(+)
- **Urothelial cancer:** p63, HMCK(+/-), AMACR(+)

(p63 image)
PCa with atrophic appearance.

CANCER WITH ATROPHIC PATTERN

PIN – LIKE PCa
12 cores, only 1 positive core with 2 atypical ducts
EQUIVOCAL IHC

- Results not entirely complimentary
  - Unexpected basal cell layer staining
  - Results supportive but all glands in an already small or difficult focus not represented in the IHC
HGPIN + ASAP

p63, HMWCK and AMACR cocktail
Atrophic/basloid – aberrant p63 (+)
ERG Immunohistochemistry

- 60% of PCa harbor any ETS-rearrangement
- 50% of PCa – TMPRSS2-ERG
- Detection by IHC or FISH
  - High concordance in hormone naive
- IHC detection in ~30% in needle setting
- Do we need a 4th marker?
  - Helps in about 5% of cases with equivocal triple cocktail
- Additional: Marker of prostate histogenesis
Post-treatment Prostate Cancer

- Recommended panel
  - CK – to detect isolated PCa cells
  - PIN cocktail (or HMCK/p63+/− racemase) – to confirm malignancy
  - Biologic potential of cancer – MIB1 (investigational)

IHC IN KIDNEY SURGICAL PATHOLOGY

- Confirming Renal origin
- Histologic subtyping of RCC

Metastatic sites
Primary tumors
Small biopsies and FNAS

PEComa
Urothelial Ca
Adrenocortical Ca
Melanoma
CONFIRMING RENAL ORIGIN

Carcinoma of unknown origin or patient with history of RCC:
- Lymph node
- Lung
- Liver
- Bone
- Other

"Unusual carcinoma" in the kidney
- Epithelioid PEComa
- Urothelial Carcinoma

Metastatic carcinoma to the kidney
  versus
  - Poorly differentiated, high grade RCC (unclassified)
  versus
  - Lymphoma, sarcoma, melanoma, other

APPROACH TO APPLICATION OF IHC IN RENAL TUMORS

Is the neoplasm a carcinoma?:
rule out Epi AML (PEComa), lymphoma, sarcoma, melanoma etc

Is the carcinoma a renal primary?:
rule out urothelial carcinoma, metastasis

Can you subtype the renal cell carcinoma?:
Clear cell vs papillary vs chromophobe vs oncocytoma vs translocation associated Ca.....

CONFIRMING RENAL ORIGIN

Is the neoplasm a carcinoma?:
- Renal "related"
  * AE1/AE3 (+)
  * EMA (+)
  * Vimentin (+)
  * CK7 (-), CK20 (-)

Is the carcinoma a renal primary?:
- Renal associated
  * RCC marker" (80%)
  * PAX 2 or PAX8 (>90%)
  * S100A1*
  * CD10 (+) (94%)
If history of renal mass and renal histogenesis markers are negative?

- Consider: Chromophobe carcinoma
  - CD117 (+) and Ksp-Cadherin (+)
- Consider: Epithelioid PEComa and translocation carcinoma
  - Cathepsin K, MelanA/HMB45

RCC antigen

- Monoclonal antibody against brush border of healthy PCT

RCC types
- Clear cell RCC (85%)
- Papillary RCC (95%)
- Oncocytoma & Chromophome (-/+)
- Collecting duct Ca (-/+)

Other tumors
- Breast ca
- Parathyroid ca
- Embryonal ca, testis
- Lung
- Prostate
- Ovary
- Melanoma
- Epididymal cystadenoma
- Mesothelioma

- CD10
### PAX2

**Pax2** is a transcription factor - normal organogenesis of the kidney, Mullerian organs, brain, eye during fetal life.

#### RCC types
- Clear cell RCC (>95%)
- Papillary RCC (>95%)
- Wilms tumor
- Metanephric (+) adenoma
- Oncocytoma (+)
- Chromophobe RCC (-/+)
- Collecting duct Ca (-/+)
- Translocation assoc. Ca (-/+)

#### Other tumors
- Nephrogenic adenoma
- Parathyroid adenoma & carcinoma
- Clear cell adenocarcinoma
- Uterine and ovarian serous and endometrioid tumors
- Adnexal tumors
- Breast carcinomas
- Lung tumors
- Colonic malignancies
- Lymphoma
- Melanoma
- Prostate carcinoma

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### PAX8

Paired box transcription factor, similar to PAX2. Predominantly data from polyclonal antibody – new monoclonal.

#### RCC types
- Clear cell RCC (>95%)
- Papillary RCC (>95%)
- Wilms tumor
- Metanephric (+) adenoma
- Oncocytoma (+)
- Chromophobe RCC (-/+)
- Collecting duct Ca (-/+)
- Translocation assoc. Ca (-/+)

#### Other tumors
- Similar to Pax2
- Thyroid neoplasms
- Extensive GYN positivity

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### Metastatic Clear cell RCC (Bone)

85% of met RCC are PAX 2 (+)
PARATHYROID CARCINOMA

PAX-2

Clear cell RCC

Papillary RCC

PAX 2

S100A1

Among the 13 member S100 protein family. Expressed in numerous cell types, not well studied

Positive in RCC
- Clear cell RCC (60%)
- Pap RCC (80%)
- Clear cell-pap RCC
- Oncocytoma
- Translocation assoc RCC
- Chromophobe RCC (-)

Other tumors
- Ovarian Ca (serous, clear)
- Endometrial Ca

-
Carbonic anhydrase IX

- Family of zinc containing metalloproteinase that regulates cell proliferation, adhesion and metastasis

<table>
<thead>
<tr>
<th>Kidney tumors</th>
<th>Other tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Clear cell RCC (+)</td>
<td>Most carcinomas of endometrium, stomach, lung, cervix, liver, breast etc.</td>
</tr>
<tr>
<td>• Papillary RCC (+/-)</td>
<td></td>
</tr>
<tr>
<td>• Chromophobe RCC (-)</td>
<td></td>
</tr>
<tr>
<td>• Oncocytoma (-)</td>
<td></td>
</tr>
<tr>
<td>• Urothelial Ca (+/-)</td>
<td></td>
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</tbody>
</table>

Prognostic utility of CA IX in clear cell RCC

Carbonic Anhydrase IX – Predictive/Prognostic

- Prognostic value: controversial with some studies showing low expression (<=85%) correlated with worse overall survival in metastatic RCC
  - High CAIX expression (>85%) predictive of response to IL-2, but final results are awaiting a prospective phase 2 SELECT trial
  - High CAIX expression (>85%) associated with more tumor shrinkage in response to Sorafenib treatment
CARBONIC ANHYDRASE IX

CLEAR CELL

PAPILLARY RCC

Ksp-cadherin in distal convoluted tubules
Chromophobe RCC

Ksp-cadherin

Oncocytoma

Chromophobe RCC

Cathepsin K

* Expression is related to overexpression of MiTF
* PEComas: moderate to strong and diffuse cytoplasmic staining is seen in all variants
  * Co-expressed with other melanocytic markers (more diffuse than HMB-45)
* MITF-TFE3 translocation associated carcinomas
  * t(X;1): >85% cases, diffuse
  * t(X;17): 0%
  * t(6;11): 100% of cases, diffuse

Other renal tumors:
Negative except nonspecific in necrotic areas

Cathepsin K

PEComa (E-AML)
Histologic subtyping of renal epithelial tumors

- Clear RCC vs. Chromophobe RCC:
  - CA-9, PAX2/8, RCC, vimentin, CD10 vs. Ksp-cadherin, CD117
- Clear RCC vs. Papillary RCC
  - CK7 and racemase

Renal Oncocytic Tumors

<table>
<thead>
<tr>
<th>Oncocytoma</th>
<th>Chromophobe RCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK 7 (- / +)</td>
<td>CK 7 (+ / -)</td>
</tr>
<tr>
<td>EPCAM (- / +)</td>
<td>EPCAM (+/-)</td>
</tr>
<tr>
<td>PAX -2 (+)</td>
<td>PAX -2 (-/+)]</td>
</tr>
<tr>
<td>Claudin 7 (-)</td>
<td>Claudin 7 (+)</td>
</tr>
<tr>
<td>S100 A1 (+)</td>
<td>S100A1 (-)</td>
</tr>
</tbody>
</table>

Amylase 1A (AMY1A) and Caveolin 1 - Investigational

*Not adequately studied: preliminary data
Not tested in hybrid oncocytic tumors*

Histologic subtyping of renal epithelial tumors

- Papillary RCC vs Metanephric adenoma
  - CK 7, racemase vs WT1, CD57
- Papillary, MTS cell ca:
  - CK7, Racemase (both+ in both tumors)
- Conv. RCC vs. Translocation carcinoma:
  - Keratin, Cathepsin K, TFE3, TFEB, MelanA/HMB-45
Renal Clear and Papillary Tumors

<table>
<thead>
<tr>
<th>Clear cell &amp; Papillary RCC</th>
<th>Papillary RCC only</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC (+)</td>
<td>RCC (+)</td>
</tr>
<tr>
<td>Pax2, Pax8 (+)</td>
<td>CK7 (+)</td>
</tr>
<tr>
<td>Vimentin (+)</td>
<td>Racemase (+)</td>
</tr>
<tr>
<td>CA-9 (+)</td>
<td>Clear – Papillary RCC</td>
</tr>
<tr>
<td>CK7 &amp; racemase (-)</td>
<td>CK 7 (+)</td>
</tr>
<tr>
<td></td>
<td>Racemase (-)</td>
</tr>
<tr>
<td></td>
<td>RCC (-)</td>
</tr>
<tr>
<td></td>
<td>HMCK (+)</td>
</tr>
</tbody>
</table>

TESTIS IHC: Screening panels

- **Germ cell tumors**
  - OCT 3/4
  - SALL4
  - PLAP
  - EMA(-)
  - Vimentin (-)

- **Sex cord tumors**
  - SF1
  - Melan A
  - Inhibin
  - Calretinin
  - CD99
  - Synaptophysin
  - S-100

- **Lymphoma:** CD-45, CD3, L26
- **Visceral malignancy:** EMA (+), vimentin (+)
LEYDIG CELL TUMOR

INHIBIN

SERTOLI CELL TUMOR

CALRETININ

IHC in characterizing the different germ cell components

- There is no substitute to well (overnight) fixed sections
- Adequate sampling is key - the # of IHCs should NEVER exceed the H&E slides
- Remember what matters in germ cell tumors
GERM CELL TUMOR – What really matters?

One does not necessarily have to characterize every morphologically different focus

- Pure classic Seminoma vs. non-seminomatous components
- Mixed germ cell tumor
  - Specify components (as accurately as you can)
  - >80% or pure embryonal carcinoma (↓)
  - >50% teratoma (↑)

Vascular-lymphatic invasion – pathologic stage
Margin status

IHC IN GERM CELL TUMORS

- **ITGCN**: Oct3/4, c-kit SALL4, Podoplanin, PLAP
- **Seminoma**: Oct3/4, c-kit, Podoplanin
- **Embryonal Ca**: Oct3/4, CD30, Keratin weak, SOX2
- **YST**: Glypican, AFP, Keratin strong
- **CC**: HPL, βHCG, Glypican-syncytiotrophoblasts

*Cytokeratin AE1/AE3*: E Ca, YST, T, CC
*Oct 3/4*: Seminoma, E Ca
*PLAP*: Minimal / no value – except in ITGCN

Useful Antibodies for Testicular Neoplasms:

- **SALL4**
  - Zinc finger nuclear transcription factor with role in embryonic development
  - ~100% sensitive for IGCNU, seminoma, EC & YST; 69% of CCs & 52% of teratomas
  - Negative in other testis tumors
  - Other + tumors: ALCL, rhabdoid tumor, Wilms tumor, precursor B-cell ALL, AML & ~ 5% of GI tract adenocarcinoma
  - Caveat: Non-neoplastic germ cells are +
  - Overview: Sensitive general GCT marker valuable for GCT vs non-GCT of testis and in DX of metastatic GCTs; sensitive YST marker, unlike OCT4
Useful Antibodies for Testicular Neoplasms:
SOX2 (SRY-box 2)

- Member of the SOX family of nuclear transcription factors involved in embryonic development; needed for pluripotency of undifferentiated embryonic stem cells
- Positive in 96% of ECs & <1% of seminomas
- Negative in YSTs, CCs & IGCNU
- Other nuclear + tumors: immature elements in teratoma, melanoma & rhabdoid tumors
- Caveat: Non-neoplastic Sertoli cells are +
- Overview: Mostly useful for seminoma vs EC. May become a preferred marker for seminoma vs EC but the panelists considered it currently technically difficult
### Glypican-3 expression in testicular germ cell tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yolk sac tumor</td>
<td>100%</td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
<td>0-8%</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>30-100%</td>
</tr>
<tr>
<td>Teratoma (*)</td>
<td>0-40%</td>
</tr>
<tr>
<td>Seminoma</td>
<td>0%</td>
</tr>
<tr>
<td>ITGCN</td>
<td>0%</td>
</tr>
</tbody>
</table>
Pitfall: normal spermatogonia in adult testis

Oct 3 more specific for ITGCN
**GERM CELL TUMORS - IHC**

*Intratubular germ cell neoplasia*
- Oct 3/4 (+)
- c-kit (+)
- Podoplanin (+)
- PLAP (+)

*Classic seminoma*
- Oct 3/4, c-kit, & Podoplanin (+)
- AE1/AE3, CAM 5.2: usually (-) (or focal)
- Sox2 (-)
- CD30: usually (-) (or focal)
- AFP: (-)

*Spermatocytic seminoma*
- Negative for most markers except CD117 (+/-).

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**GERM CELL TUMORS - IHC**

*Embryonal carcinoma*
- AE1/AE3, CAM 5.2: (+)
- CD30: (+)
- Oct 3/4 (+)
- Sox2 (+)
- AFp: (-)
- c-kit (-)

*Endodermal sinus tumor (YST)*
- AE1/AE3, CAM 5.2: (+)
-AFP: (+)
- Glypican 3 (+)
- CD30 (Ber-H2): (-)
- c-kit: (-)
- Oct 3/4 (-)

**Choriocarcinoma**
- AE1/AE3, CAM 5.2: (+)
- hHCG: (+)
- Human placental lactogen: (+)
- Oct 3/4 (-)

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**SEMINOMA**

- PLAP
- OCT3
- CKIT
Spermatocytic seminoma: (-) for Oct3/4
Weak CD117 and SALL4

Seminoma: Classic vs Spermatocytic

- Weak CD117
- SALL4
Useful Antibodies for Testicular Neoplasms: Glypican 3 (GPC3)

- Membrane anchored heparan sulfate proteoglycan
- Positive in YSTs (100%), CCs (80%), teratomas ("immature") (17%) & rare ECs (5%)
- Negative in IGCNU & seminoma
- Other + tumors: hepatocellular and gastric cancers
- Caveats: Syncytiotrophoblast cells are often positive (71%)
- Overview: More sensitive but less specific for YST among testis GCTs than AFP