#### Metastatic breast carcinoma

| Antibody                        | Reference    | Breast carcinomas   | Positive in other neoplasia  |
|---------------------------------|--------------|---|--|
| GATA3 (L50-823)                 | MAD-000632QD | 96% but less sensitive for TNC  | Urothelialandsquamouscarcinomasamong others  |
| GCDFP-15/BRST-2<br>(EP95)       | MAD-000742QD | - 80% of tumors<br>-Higher sensitivity for lobular<br>carcinomas            | Normal and neoplastic tissues with a pocrine differentiation                         |
| Mammaglobin<br>(304-1A5 Y 31A5) | MAD-000340QD | - More than 70% of tumors<br>- Higher sensitivity for lobular<br>carcinomas | Endocervical and endometrial normal and neoplastic tissue                            |
| EstrogenReceptor (SP1)          | MAD-000306QD | Higher positive rate in well differentiated carcinomas                      | Frequentlypositiveingynecologicneoplasms among others                                |
| PAX8 (PAX8/1492)                | MAD-000753QD | Negative  | Ovarian, renal, thyroid and parathyroid  |
| TTF1 (SPT24)                    | MAD-000486QD | 2,5% of the cases   | Lung and thyroid (papillary) carcinomas  |
| WT1 (6F-H2)                     | MAD-005671QD | Negative  | Nefroblastoma, Wilm´stumor, DSRCT, normal mesothelium and tumors, ovarian carcinomas |
| Napsin A (BS10)                 | MAD-000752QD | Negative  | Some lung, renal, thyroid, ovarian carcinomas  |

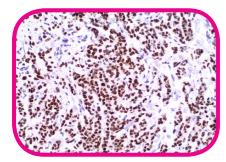


Photo 13: GATA3 nuclear staining in a lymphnode metastasis from a no ccult ductal carcinoma

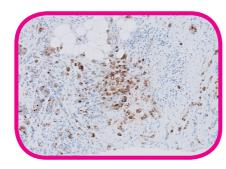


Photo14:GCDFP-15(BRST2):staining in apocrine metastatic carcinoma

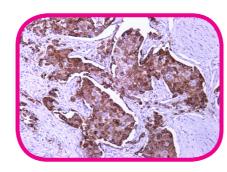


Photo 15: Mammoglobin cytoplasm staining in a ductal carcinoma

#### Chief references

- Peng Y, Butt YM, Chen B, Zhang X, Tang P. Update on Immunohistochemical Analysis in Breast Lesions. Arch Pathol Lab Med. 2017 Jun 2. doi: 10.5858/arpa.2016-0482-RA
- Liu H. Application of immunohistochemistry in breast pathology: a review and update. Arch Pathol Lab Med. 2014 Dec;138(12):1629-42



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# Immunohistochemistry in breast lesions

## Prognostic markers

| Antibody              | Reference    | Luminal A and normal-like | Luminal B | HER2+    | TNC* |
|-----------------------|--------------|---------------------------|-----------|----------|------|
| ER <sup>†</sup> (SP1) | MAD-000306QD | +                         | +         | -        | -    |
| PR <sup>‡</sup> (16)  | MAD-000670QD | variable                  | variable  | -        | -    |
| CerbB2 (SP3)          | MAD-000308QD | -                         | -/+       | +        | -    |
| Ki67 (SP6)            | MAD-000310QD | low                       | high      | high     | high |
| p53 (SP5)             | MAD-000309QD | variable                  | variable  | variable | +    |

<sup>\*</sup> TNC – triple negative carcinomas

**<sup>‡</sup> Progesterone Receptors** 

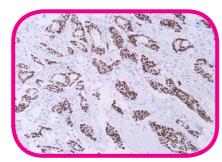


Photo1.Estrogenreceptorinaluminal A ductal carcinoma

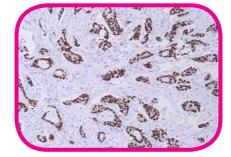


Photo 2. Progesterone receptor in a luminal A ductal carcinoma

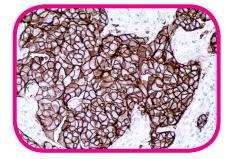


Photo 3. Her2 3+ staining in a HER2 positive ductal carcinoma



<sup>†</sup> Estrogen Receptors

• Distinguish between usual ductal hyperplasia (UDH) and atypical ductal hyperplasia/low-grade ductal carcinoma in situ (ADH/LGDCIS)

| Antibody                  | Reference    | UDH           | ADH/LGDCIS*        |
|---------------------------|--------------|---------------|--------------------|
| Cytokeratin5/6(EP67+EP24) | MAD-000651QD | heterogeneous | negative           |
| Cytokeratin 34betaE12     | MAD-009059QD | heterogeneous | negative           |
| Estrogen Receptor (SP1)   | MAD-000306QD | heterogeneous | diffusely positive |

<sup>\*</sup>basal like DCIS can mimic UDH and be positive for CK5/6 in either a diffuse or patchy pattern

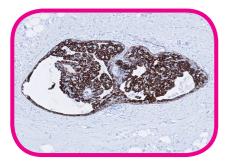


Photo 4. Cytokeratin 5/6 diffuse staining in a UDH



Photo5.Cytokeratin34betaE12diffuse staining in a UDH

• Differentiate between invasive and "in situ" carcinomas - demonstrate the presence of mioepithelial cells\*

| Antibody                                     | Reference    | Invasive carcinoma | "In situ" carcinomas |
|--|--------------|--------------------|----------------------|
| p63 (4A4)                                    | MAD-000479QD | absent             | present              |
| Smooth muscle myosin,<br>heavy chain (EP166) | MAD-000718QD | absent             | present              |
| Calponin (EP63)                              | MAD-000658QD | absent             | present              |
| Smoothmuscleactin (1A4)                      | MAD-001195QD | absent             | present              |
| CD10 (56C6)                                  | MAD-002022QD | absent             | present              |
| S100 (4C4.9)                                 | MAD-001221QD | absent             | present              |
| Podoplanin (D2-40)                           | MAD-000402QD | absent             | present              |
| Cytokeratin5/6(EP67+EP24)                    | MAD-000651QD | absent             | present              |
| Cytokeratin 14 (LL02)                        | MAD-005103QD | absent             | present              |

<sup>\*</sup> adenoid cystic carcinomas and metaplastic carcinomas might express mioepithelial markers

<sup>\*</sup> they might be also useful to differentiate papillary lesions

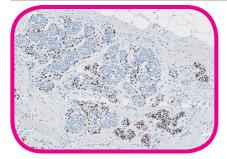


Photo 6: p63 highlighting the mioepithelial cells in an "in situ" lobular neoplasia



Photo7:Smoothmusclemyosin,heavy chain staining myoepithelial cells of normal breast ducts



Photo 8: Calponin, highlighting the myoepithelial cells of an "in situ" ductal carcinoma

### Distinguish between ductal and lobular lesions

BREAST

| Antibody                   | Reference    | Ductal              | Lobular              |
|----------------------------|--------------|---------------------|----------------------|
| E-cadherin (BS38)          | MAD-000643QD | Positive            | Negative             |
| Delta-cathenin(p120)(EP66) | MAD-000724QD | Membrane positivity | Cytoplasm positivity |
| Cytokeratin 34betaE12      | MAD-009059QD | Absent              | Cytoplasm positivity |

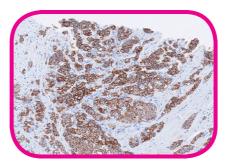


Photo 9: E-cadherin membrane staining in a ductal carcinoma with trabecularandisolated cells pattern of infiltration

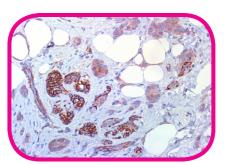


Photo 10: Delta-cathenin (p120) cytoplasmstaininginlobularinfiltrating carcinomawhilenormalductsshows membrane staining

## • Characterize triple negative-carcinomas

| Antibody                   | Reference    | TNC*                                     |
|----------------------------|--------------|--|
| Androgenreceptors (SP107)  | MAD-000710QD | +/-                                      |
| EGFR (EP22)                | MAD-000664QD | + majority of basal-like TNC             |
| p53 (SP5)                  | MAD-000309QD | + majority of basal-like TNC             |
| p16 INK4A (RUO) (MX007)    | MAD-000690QD | + in more than 70% of basal-like TNC     |
| Cytokeratin5/6 (EP67+EP24) | MAD-000651QD | More than 60% of the basal-like TNC      |
| Cytokeratin 14 (LL02)      | MAD-005103QD | More than 60% of the basal-like TNC      |
| GATA3 (L50-823)            | MAD-000632QD | 43% to 66% of the cases                  |
| E-cadherin (BS38)          | MAD-000643QD | Partially lost in poor prognosis tumors  |
| Cyclin-E1 (EP126)          | MAD-000713QD | High expression in poor prognosis tumors |

<sup>\*</sup>TNC – triple negative carcinomas

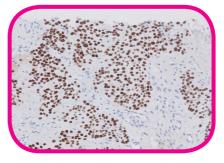


Photo11:p53diffusenuclearstaining in a TNC

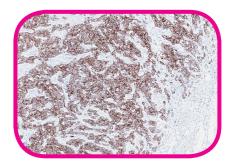


Photo 12: CK5/6 diffuse membrane staining in a TNC

 $<sup>*</sup>microglandular adenosis has no myoepithelial cells and the cells generally express {\tt S100} protein and are negative for {\tt ER} and {\tt PR}$