

**Supplementary Digital Content S1: Search strategy in EMBASE via OVID until July 2019 with daily update.**

('ovary tumor'/exp OR 'ovarian neoplasia' OR 'ovarian neoplasm' OR 'ovarian neoplasms' OR 'ovarian tumor' OR 'ovarian tumour' OR 'ovarium tumor' OR 'ovarium tumour' OR 'ovary neoplasm' OR 'ovary tumor' OR 'ovary tumor treatment' OR 'ovary tumour' OR 'ovary tumour treatment' OR 'epithelial ovarian carcinoma'/exp OR 'fallopian tube cancer'/exp OR 'primary peritoneal carcinoma'/exp OR 'primary peritoneal cancer'/exp OR 'primary peritoneal serous carcinoma'/exp OR 'ovary cancer'/exp OR 'cancer, ovary' OR 'malignant ovary tumor' OR 'malignant ovary tumour' OR 'ovarial cancer' OR 'ovarian cancer' OR 'ovarium cancer' OR 'ovary cancer') AND (brca OR 'tumor suppressor gene'/exp OR 'brca1 gene' OR 'cancer suppressor gene' OR 'cancer suppressor genes' OR 'genes, brca2' OR 'genes, brca1' OR 'genes, suppressor, tumor' OR 'genes, suppressor, tumour' OR 'genes, tumor suppressor' OR 'genes, tumour suppressor' OR 'tumor suppressor gene' OR 'tumor suppressor genes' OR 'tumour suppressor gene' OR 'tumour suppressor genes' OR 'brca1 protein'/exp OR 'brca2 protein'/exp OR 'brca1 associated ring domain protein 1'/exp OR 'brca2 gene'/exp OR 'brca1 protein human'/exp OR 'brca2 protein human'/exp OR 'brca gene'/exp OR 'brca protein'/exp) AND ('immunohistochemistry'/exp OR 'antigen staining' OR 'histochemistry, immuno' OR 'immunohistochemistry' OR 'immunostaining' OR 'staining, antigen' OR immunohistochemistry)

**Supplemental Digital Content S2: Search strategy in MEDLINE via PubMed until July 2019 with daily update.**

(((((ovarian neoplasm[MeSH Terms]) OR (((((((((((((((Neoplasm, Ovarian) OR Ovarian Neoplasm) OR Ovary Neoplasms) OR Neoplasm, Ovary) OR Neoplasms, Ovary) OR Ovary Neoplasm) OR Neoplasms, Ovarian) OR Ovary Cancer) OR Cancer, Ovary) OR Cancers, Ovary) OR Ovary Cancers) OR Ovarian Cancer) OR Cancer, Ovarian) OR Cancers, Ovarian) OR Ovarian Cancers) OR Cancer of Ovary) OR Cancer of the Ovary))) OR (((ovarian) OR Ovaries) OR Ovary[MeSH Terms])) AND (((((((((((((((Neoplasms[MeSH Terms]) OR (((((((((((((((Neoplasia) OR Neoplasias) OR Neoplasm) OR Tumors) OR Tumor) OR Malignancy) OR Malignancies) OR Cancer) OR Cancers)) OR Carcinoma[MeSH Terms]) OR (((((((((((((((Carcinomas) OR Epithelial Neoplasms, Malignant) AND Malignant Epithelial Neoplasms) AND Epithelial Neoplasm, Malignant) AND Malignant Epithelial Neoplasm) AND

Neoplasm, Malignant Epithelial) AND Neoplasms, Malignant Epithelial) AND Epithelial Tumors, Malignant) AND Epithelial Tumor, Malignant) AND Malignant Epithelial Tumor) AND Malignant Epithelial Tumors) AND Tumor, Malignant Epithelial) AND Tumors, Malignant Epithelial)) OR Fallopian Tube Neoplasms[MeSH Terms]) OR (((((((Fallopian Tube Neoplasm) OR Neoplasm, Fallopian Tube) OR Neoplasms, Fallopian Tube) OR Fallopian Tube Cancer) OR Cancer, Fallopian Tube) OR Cancers, Fallopian Tube) OR Fallopian Tube Cancers) OR Cancer of the Fallopian Tube)) OR Peritoneal Neoplasms[MeSH Terms]) OR (((Neoplasm, Peritoneal) OR Neoplasms, Peritoneal) OR Peritoneal Neoplasm)))) AND (((((((Genes, BRCA1[MeSH Terms]) OR (((BRCA1 Genes) OR Gene, BRCA1) OR BRCA1 Gene)) OR BRCA1 Protein[MeSH Terms]) OR (((Breast Cancer Type 1 Susceptibility Protein) OR Breast Cancer 1 Protein) OR Ring Finger Protein 53) OR BRCA1 Gene Product) OR Breast Cancer 1 Gene Product)) OR (((BRCA2 Genes) OR Gene, BRCA2) OR BRCA2 Gene)) OR BRCA2 Protein[MeSH Terms]) OR (((((((FANCD1 Protein) OR Fanconi Anemia Complementation Group D1 Protein) OR Fanconi Anemia Group D1 Protein) OR BRCA2 Gene Product) OR Breast Cancer 2 Gene Product) OR Fanconi Anemia Group D1 Complementing Protein) OR Breast Cancer 2 Protein))) AND ((Immunohistochemistry[MeSH Terms]) OR Immunohistochemistry).

**Supplementary Digital Content S3: Search strategy in Web of Science until July 2019 with daily update.**

((fallopian tube) AND (cancer\* or neoplas\* or carcinoma\* or tumor\* or tumour\* or malignan\*) OR (primary peritoneal) AND (cancer\* or neoplas\* or carcinoma\* or tumor\* or tumour\* or malignan\*) OR (ovar\*) AND (cancer\* or neoplas\* or carcinoma\* or tumor\* or tumour\* or malignan\*)) AND (("brca\*") OR ("brca? protein") OR ("brca? gene") OR ("Breast Cancer Type ? Susceptibility Protein") OR ("Breast Cancer ? Protein") OR ("Breast Cancer? Gene Product")) AND ("IHC\*") OR ("immunohistochemi\*"))).

**Supplementary Digital Content S4: Search strategy in Scopus until July 2019 with daily update.**

(( (title-abs-key ( ovar\* ) ) and ( (title-abs-key ( cancer\* ) or title-abs-key ( carcinoma\* ) or title-abs-key ( neoplas\* ) or title-abs-key ( malignan\* ) or title-abs-key ( tumor\* ) or title-abs-

key ( tumour\* ) ) ) or ( ( title-abs-key ( "fallopian tube" ) ) and ( ( title-abs-key ( cancer\* ) or title-abs-key ( carcinoma\* ) or title-abs-key ( neoplas\* ) or title-abs-key ( malignan\* ) or title-abs-key ( tumor\* ) or title-abs-key ( tumour\* ) ) ) ) or ( ( ( title-abs-key ( cancer\* ) or title-abs-key ( carcinoma\* ) or title-abs-key ( neoplas\* ) or title-abs-key ( malignan\* ) or title-abs-key ( tumor\* ) or title-abs-key ( tumour\* ) ) ) and ( title-abs-key ( "primary peritoneal" ) ) ) ) and ( ( title-abs-key ( "brca\*" ) ) or ( ( title-abs-key ( "brca? protein" ) or title-abs-key ( "brca? gene" ) ) ) or ( ( title-abs-key ( "breast cancer ? susceptibility protein" ) or title-abs-key ( "breast cancer ? protein" ) or title-abs-key ( "breast cancer ? gene product" ) ) ) ) and ( ( title-abs-key ( "ihc" ) or title-abs-key ( "immunohistochemi\*" ) ) ) ).

## Supplementary Digital Content S5 Excluded studies and reasons.

| First author (Year) | Journal                     | Identifier                             | Reason of exclusion   |
|---------------------|-----------------------------|--|-----------------------|
| Aghmesheh (2004)    | <i>Gynecol Oncol</i>        | DOI:10.1016/j.ygyno.2004.08.035        | No IHC                |
| Altaras (2002)      | <i>Gynecol Oncol</i>        | DOI:10.1006/gyno.2001.6492             | No IHC                |
| Bi (2013)           | <i>J Ovarian Res</i>        | DOI:10.1186/1757-2215-6-89             | No enough information |
| Bruchim (2004)      | <i>Int J Gynecol Cancer</i> | DOI:10.1111/j.1048-891X.2004.014208.x  | No IHC                |
| Busacca (2012)      | <i>J Pathol</i>             | DOI:10.1002/path.3979                  | No EOC                |
| Cass (2003)         | <i>Cancer</i>               | DOI 10.1002/cncr.11310                 | No IHC                |
| Cass (2005)         | <i>Obstet Gynecol</i>       | DOI:10.1097/01.AOG.0000187892.78392.3f | No IHC                |
| Clarke (2009)       | <i>Mod Pathol</i>           | DOI:10.1038/modpathol.2008.191         | Duplicate             |
| Darcy (2010)        | <i>Gynecol Oncol</i>        | DOI:10.1016/j.ygyno.2010.01.048        | Not original          |
| Fang (2014)         | <i>BMC Cancer</i>           | DOI:10.1186/1471-2407-14-188           | No enough information |
| Fedoseienko (2016)  | <i>PloS One</i>             | DOI:10.1371/journal.pone.0165385       | No IHC                |
| Garg (2013)         | <i>Am J Surg Pathol</i>     | DOI:10.1097/PAS.0b013e31826cabbd       | Duplicate             |
| Gau (2015)          | <i>Cell Cycle</i>           | DOI:10.1080/15384101.2015.1036203      | No IHC                |
| George (2011)       | <i>J Pathol</i>             | DOI:10.1002/path.2927                  | No EOC                |
| Gruessner (2014)    | <i>Am J Cancer Res</i>      | PMC:3902233                            | No IHC                |
| Haefner (2016)      | <i>Int J Cancer</i>         | DOI:10.1002/ijc.29690                  | Duplicate             |
| Kar (2007)          | <i>Cancer Biol Ther</i>     | DOI:10.4161/cbt.6.7.4329               | No enough information |

|                     |                              |   |                       |
|---------------------|------------------------------|---|-----------------------|
| Kim (2014)          | <i>Korean J Pathol</i>       | DOI:10.4132/KoreanJPathol.2014.48.5.379 | Case report           |
| Lee (2015)          | <i>Exp Mol Med</i>           | DOI:10.1038/emm.2015.85                 | No IHC                |
| Levine (2002)       | <i>Gynecol Oncol</i>         | DOI:10.1006/gyno.2002.6646              | No IHC                |
| Li (2007)           | <i>Cancer Res</i>            | DOI:10.1158/0008-5472.CAN-07-2370       | Cell lines            |
| Li (2013)           | <i>J Exp Clin Cancer Res</i> | DOI:10.1186/1756-9966-32-102            | No IHC                |
| Liu (2014)          | <i>Oncol Lett</i>            | DOI:10.3892/ol.2014.1929                | No enough information |
| Lowery (2012)       | <i>Int J Gynecol Cancer</i>  | DOI:10.1097/IGC.0b013e318231f140        | No IHC                |
| May (2013)          | <i>Neoplasia</i>             | DOI 10.1593/neo.121674                  | No enough information |
| Mehra (2011)        | <i>Mod Pathol</i>            | DOI:10.1038/modpathol.2010.171          | No EOC                |
| Milner (2013)       | <i>Virchows Arch</i>         | DOI:10.1007/s00428-012-1368-y           | Cell lines            |
| Monk (2014)         | <i>Gynecol Oncol</i>         | DOI.org/10.1016/j.ygyno.2013.10.032     | Unanswered email      |
| Muñoz-Repeto (2013) | <i>Histol Histopathol</i>    | DOI:10.14670/HH-28.133                  | No IHC                |
| Ossovskaya (2010)   | <i>Genes Cancer</i>          | DOI:10.1177/1947601910383418            | No IHC                |
| Pennington (2013)   | <i>Gynecol Oncol</i>         | DOI:10.1016/j.ygyno.2012.12.007         | No enough information |
| Press (2010)        | <i>Neoplasia</i>             | DOI:10.1593/neo.101044                  | No IHC                |
| Rao (2002)          | <i>Biotechniques</i>         | PMID:11962614                           | Cell lines            |
| Ravid (2000)        | <i>Eur J Cancer</i>          | DOI:10.1016/S0959-8049(00)00096-4       | No IHC                |
| Reyes (2014)        | <i>Mod Pathol</i>            | DOI:10.1038/modpathol.2013.237          | Duplicate             |
| Ross (2013)         | <i>Gynecol Oncol</i>         | DOI:10.1016/j.ygyno.2013.06.019         | No IHC                |

|                      |                                |                                      |                       |
|----------------------|--------------------------------|--------------------------------------|-----------------------|
| Russo (2007)         | <i>Breast Cancer Res Treat</i> | DOI:10.1007/s10549-006-9456-9        | No IHC                |
| Schofield (2000)     | <i>The Breast</i>              | DOI:10.1054/brst.1999.0090           | Case report           |
| Scully (1996)        | <i>Science</i>                 | DOI:10.1126/science.272.5258.123     | Cell lines            |
| Sekine (2012)        | <i>J Obstet Gynaecol Res</i>   | DOI:10.1111/j.1447-0756.2012.01961.x | Duplicate             |
| Shabanizadeh (2013)  | <i>Middle East J Cancer</i>    | ISSN: 2008-6709                      | Non-invasive EOC      |
| Staff (2014)         | <i>Int J Gynecol Pathol</i>    | DOI:10.1097/PGP.0b013e31829c673b     | No EOC                |
| Strathdee (2001)     | <i>Am J Pathol</i>             | DOI:10.1016/S0002-9440(10)64059-X    | No enough information |
| Sun (2013)           | <i>J Natl Cancer Inst</i>      | DOI:10.1093/jnci/djt302              | Duplicate             |
| Van der Steen (2017) | <i>Int J Gynecol Cancer</i>    | DOI:10.1097/IGC.0000000000000933     | No IHC                |
| Wang (2016)          | <i>Cancer Res</i>              | DOI:10.1158/0008-5472.CAN-16-0186    | Cell lines            |
| Werness (2000)       | <i>J Natl Cancer Inst</i>      | PMID:10880552                        | Case report           |
| Wysham (2012)        | <i>PLoS One</i>                | DOI:10.1371/journal.pone.0030042     | No IHC                |
| Zhang (2005)         | <i>Int J Gynecol Cancer</i>    | DOI:10.1111/j.1048-891X.2005.15007.x | No IHC                |
| Zhu (2015)           | <i>Oncotarget</i>              | DOI:10.18632/oncotarget.3428         | No EOC                |

IHC = Immunohistochemistry; EOC = Epithelial ovarian cancer.

**Supplementary Digital Content S6 Characteristics of included studies.**

| <b>First author (Year)[Ref.]</b> | <b>Study design</b> | <b>Inclusion period</b> | <b>Country</b>    | <b>N (invasive)</b> | <b>Histology</b> | <b>FIGO</b> | <b>IHC target</b> |
|----------------------------------|---------------------|-------------------------|-------------------|---------------------|------------------|-------------|-------------------|
| Al-Kashwan (2017)[18]            | Cohort              | 2014-2015               | Iraq              | 35                  | Mixed            | All         | BRCA1             |
| Bai (2014)[19]                   | Cohort              | 2002-2010               | China             | 142                 | Mixed            | All         | BRCA1             |
| Baldwin (2000)[20]               | Cohort              | NS                      | USA               | 98                  | Mixed            | NS          | BRCA1             |
| Carser (2011)[10]                | Cohort              | 1985-2011               | UK                | 292                 | Mixed            | All         | BRCA1             |
| Cho (2015)[21]                   | Cohort              | 1996-2008               | Republic of Korea | 104                 | Mixed            | All         | BRCA1             |
| Fernández (2017)[22]             | Cross sectional     | 2001-2014               | Venezuela         | 43                  | Mixed            | NS          | BRCA1             |
| Furukawa (2013)[23]              | Cohort              | 2005-2010               | Japan             | 14                  | PPSC             | Advanced    | BRCA1, BRCA2      |
| Gan (2013)[24]                   | Cohort              | 1991-2007               | UK                | 174                 | HGSC             | All         | BRCA1             |
| Gunes (2007)[25]                 | Cohort              | 1995-2004               | Turkey            | 58                  | Serous*          | All         | BRCA1             |
| Hjortkjær (2017)[26]             | Cohort              | 1991-1994               | Denmark           | 170                 | Mixed            | Advanced    | BRCA1             |
| Ju (2016)[27]                    | Cohort              | 2011-2014               | China             | 39                  | Mixed            | All         | BRCA1             |
| Kaern (2005)[28]                 | Cohort              | 1990-1992               | Norway            | 51                  | Mixed            | Advanced    | BRCA1             |
| Kashima (2000)[29]               | Series of cases     | NS and 1995-1998        | Japan             | 44                  | Mixed            | NS          | BRCA1             |
| Lesnock (2013)[30]               | Cohort              | 1998-2001               | USA               | 393                 | Mixed            | Advanced    | BRCA1             |
| Li (2017)[31]                    | Cohort              | 2008-2015               | China             | 209                 | Mixed            | All         | BRCA1, BRCA2      |
| McAlpine (2012)[32]              | Cohort              | 2004-2009               | Canada            | 131                 | Mixed            | All         | BRCA1             |
| McMillen (2012)[33]              | Cohort              | 2002-2007               | USA               | 117                 | Mixed            | Advanced    | BRCA1             |

|                       |                 |                         |                  |     |         |          |              |
|-----------------------|-----------------|-------------------------|------------------|-----|---------|----------|--------------|
| Meisel (2014)[12]     | Cohort          | 1996-2010               | USA              | 135 | HGSC    | Advanced | BRCA1        |
| Nomura (2016)[34]     | Cohort          | 2000-2009 and 2009-2009 | Japan and Europe | 199 | Serous* | All      | BRCA1        |
| Popovska (2014)[35]   | Cohort          | NS                      | Bulgaria         | 29  | Serous* | NS       | BRCA1        |
| Pradjatmo (2014)[36]  | Cohort          | NS                      | Indonesia        | 69  | Mixed   | All      | BRCA1        |
| Press (2008)[37]      | Cohort          | 2004-2005               | Canada           | 49  | Mixed   | NS       | BRCA1        |
| Radosa (2011)[38]     | Cohort          | 2000-2005               | Germany          | 27  | Mixed   | Advanced | BRCA1        |
| Russell (2000)[39]    | Series of cases | NS                      | UK               | 51  | Mixed   | All      | BRCA1        |
| Sallum (2018)[58]     | Cohort          | 1996-2013               | Brazil           | 106 | Serous* | All      | BRCA1        |
| Shawky (2014)[40]     | Cohort          | 2006-2007               | Egypt            | 19  | Mixed   | All      | BRCA1        |
| Shilpa (2014)[41]     | Cohort          | 2010-2012               | India            | 64  | Mixed   | All      | BRCA1        |
| Sirisabya (2007)[42]  | Cohort          | 1996-1999               | Thailand         | 99  | Mixed   | All      | BRCA1        |
| Skytte (2011)[43]     | Series of cases | NS                      | Denmark          | 54  | Mixed   | All      | BRCA1        |
| Strickland (2016)[44] | Cohort          | NS                      | USA              | 17  | HGSC    | NS       | BRCA1        |
| Sun (2015)[13]        | Cohort          | 2001-2009               | China            | 156 | HGSC    | Advanced | BRCA1, BRCA2 |
| Swisher (2009)[45]    | Cohort          | NS                      | USA              | 115 | Mixed   | All      | BRCA1, BRCA2 |
| Thrall (2006)[46]     | Cohort          | 1998-2001               | USA              | 230 | Mixed   | All      | BRCA1        |
| Vaz (2007)[47]        | Cohort          | 2000-2002               | Portugal         | 4   | Mixed   | All      | BRCA1, BRCA2 |
| Vorrius (2009)[48]    | Case-control    | NS                      | USA              | 53  | Mixed   | NS       | BRCA1, BRCA2 |
| Wang (2004)[49]       | Series of cases | NS                      | Japan            | 76  | Mixed   | All      | BRCA1        |



|                      |                 |           |        |     |              |          |              |
|----------------------|-----------------|-----------|--------|-----|--------------|----------|--------------|
| Wang L (2015)[51]    | Series of cases | 2000-2013 | China  | 67  | Mixed        | NS       | BRCA1        |
| Wang Z (2015)[50]    | Cohort          | 2005-2010 | China  | 150 | HGSC         | Advanced | BRCA2        |
| Weberpals (2011)[52] | Cohort          | 2001-2008 | Canada | 251 | Mixed        | Advanced | BRCA1        |
| Yang (2010)[53]      | Cohort          | NS        | USA    | 223 | HGSC         | NS       | BRCA2        |
| Yang (2011)[54]      | Cohort          | 1990-2006 | USA    | 51  | Endometrioid | All      | BRCA2        |
| Ye (2014)[55]        | Cohort          | 2005-2009 | China  | 97  | Serous*      | All      | BRCA1        |
| Zhang (2015)[56]     | Cohort          | 2003-2009 | China  | 161 | Mixed        | All      | BRCA1, BRCA2 |
| Zheng (2000)[57]     | Cohort          | 1995-1998 | USA    | 38  | Mixed        | NS       | BRCA1        |

\*Low and high grade; PPSC = Primary peritoneal serous cancer; HGSC = High-grade serous carcinoma; NS = Not specified

## Supplementary Digital Content S7 Immunohistochemistry method of the BRCA1 and BRCA2 target.

| Study<br>(Year)          | Sectioning<br>( $\mu\text{m}$ ) | Antigen<br>retrieval                             | Primary antibody<br>(dilution)    | Incubation time<br>(temperature °C) | Performed | Location | Score<br>system | Cut-off<br>positive | N<br>Neg/total (%) |
|--------------------------|---------------------------------|--|-----------------------------------|-------------------------------------|-----------|----------|-----------------|---------------------|--------------------|
| <b>BRCA1</b>             |                                 |  |                                   |                                     |           |          |                 |                     |                    |
| Al-Kashwan<br>(2017)[18] | WS (5)                          | Citrate buffer,<br>DakoCytomation,<br>water-bath | Dako GLK-2<br>(1:50)              | 30 min (37)                         | Manual    | Both     | P + I           | H-score<br>>47      | 23/28 (82.2%)      |
| Bai<br>(2014)[19]        | WS (4)                          | Sodium citrate,<br>heat                          | Merck Calbiochem<br>MS110 (1:100) | Overnight (4)                       | Manual    | Nucleus  | P + I           | Any                 | 67/142 (47.2%)     |
| Baldwin<br>(2000)[20]    | WS (NS)                         | Dako solution,<br>heat                           | Oncogene MS110<br>(1:150)         | Overnight (4)                       | Manual    | Nucleus  | I               | 0                   | 14/21 (66.6%)      |
| Carser<br>(2011)[10]     | WS (3)                          | Pressure cooker                                  | Merck Calbiochem<br>MS110 (1:200) | Overnight (4)                       | Manual    | Nucleus  | P               | >10%                | 120/292 (41.0%)    |
| Cho<br>(2015)[21]        | TMA (4)                         | Sodium citrate,<br>microwave                     | Abcam MS110<br>(1:100)            | (NS) (NS)                           | Manual    | Nucleus  | P + I           | Any                 | 58/104 (55.7%)     |
| Fernández<br>(2017)[22]  | TMA (4)                         | Citrate, water<br>bath                           | (NS) MS110 (NS)                   | (NS) (NS)                           | Manual    | Both     | P               | >10%                | 15/43 (34.9%)      |
| Furukawa<br>(2013)[23]   | NS (NS)                         | NS   | Merck MS110<br>(NS)               | (NS) (NS)                           | Manual    | NS       | P               | $\geq$ 10%          | 2/14 (14.3%)       |

|                         |         |                               |  |               |                         |         |       |                |                 |
|-------------------------|---------|-------------------------------|--|---------------|-------------------------|---------|-------|----------------|-----------------|
| Gan<br>(2013)[24]       | TMA (4) | Citrate,<br>microwave         | Merck Calbiochem<br>MS110 (1:80)           | 60 min (NS)   | Manual and<br>automated | Nucleus | P + I | H-score<br>>70 | 117/139 (84.2%) |
| Gunes<br>(2007)[25]     | WS (4)  | NS                            | NeoMarkers GLK-<br>2 (NS)                  | (NS) (NS)     | Manual                  | Both    | P + I | Any            | 19/58 (32.7%)   |
| Hjortkjær<br>(2017)[26] | WS (4)  | TEG, microwave                | Calbiochem<br>MS110 (1:600)                | Overnight (4) | Manual                  | Nucleus | P     | >10%           | 65/170 (38.2%)  |
| Ju<br>(2016)[27]        | WS (4)  | EDTA, heat<br>pressure cooker | (NS) Anti-BRCA1<br>(NS)                    | Overnight (4) | Manual                  | Both    | P + I | Any            | 31/39 (79.5%)   |
| Kaern<br>(2005)[28]     | WS (5)  | Citrate,<br>microwave         | Oncogene MS110<br>(1:200)                  | 30 min (NS)   | Manual                  | Nucleus | P     | ≥10%           | 30/46 (65.2%)   |
| Kashima<br>(2000)[29]   | WS (5)  | NS                            | Phenopath<br>Laboratory GLK-2<br>(1:10000) | Overnight (4) | Manual                  | Both    | P + I | Any            | 10/44 (22.7%)   |
|                         | WS (5)  | NS                            | Oncogene Ab-2<br>(1:10)                    | Overnight (4) | Manual                  | Both    | P + I | Any            | 7/44 (15.9%)    |
| Lesnock<br>(2013)[30]   | WS (5)  | NS                            | Oncotech MS110<br>(NS)                     | (NS) (NS)     | Manual                  | Nucleus | P     | >10%           | 189/393 (48.1%) |
| Li<br>(2017)[31]        | TMA (5) | Citrate, heat                 | Proteintech 20649-<br>1-AP rabbit (1:300)  | 14 h (4)      | Manual                  | NS      | P + I | Any            | 132/205 (64.4%) |

|                         |                    |                                      |   |                              |                         |         |       |      |                |
|-------------------------|--------------------|--------------------------------------|---|------------------------------|-------------------------|---------|-------|------|----------------|
| McAlpine<br>(2012)[32]  | TMA (4)            | Std CC2,<br>UltraMap Kit             | Calbiochem<br>MS110 (1:10, 1:25,<br>1:50, 1:75) | (NS) (NS)                    | Manual and<br>automated | Nucleus | P     | >1%  | 59/131 (45.0%) |
| McMillen<br>(2012)[33]  | TMA (4)            | NS                                   | EMD Calbiochem<br>MS110 (NS)                    | (NS) (NS)                    | Manual and<br>automated | NS      | I     | Any  | 54/105 (52.4%) |
| Meisel<br>(2014)[14]    | TMA and<br>WS (NS) | EDTA, heat                           | Merck Calbiochem<br>MS110 (1:100)               | (NS) (NS)                    | Manual                  | Nucleus | P     | >10% | 48/135 (35.5%) |
| Nomura<br>(2016)[34]    | WS (4)             | Dako, heat                           | Merck Anti-<br>BRCA1(1:100)                     | 1 h (Room<br>temperature)    | Manual and<br>automated | Nucleus | P + I | ≥10% | 75/199 (37.7%) |
| Popovska<br>(2014)[35]  | WS (4)             | Dako solution,<br>microwave          | Abcam MS110<br>(1:50)                           | 30 min (Room<br>temperature) | Manual                  | Both    | P     | >10% | 19/29 (65.5%)  |
| Pradjatmo<br>(2014)[36] | WS (3-5)           | NS                                   | Biocare Medical<br>MS110 (NS)                   | (NS) (NS)                    | Manual                  | Nucleus | P     | ≥10% | 47/69 (68.1%)  |
| Press<br>(2008)[37]     | WS (NS)            | EDTA,<br>microwave and<br>water bath | Oncogene MS110<br>(1:50)                        | (NS) (NS)                    | Manual and<br>automated | Nucleus | P     | >1%  | 23/49 (47.0%)  |
| Radosa<br>(2011)[38]    | WS (NS)            | Citrate, heat                        | Merck MS110<br>(1:200)                          | Overnight (4)                | Manual                  | Nucleus | P + I | >10% | 12/27 (44.5%)  |

|                         |          |                                     |   |                               |                         |           |       |      |                |
|-------------------------|----------|-------------------------------------|---|-------------------------------|-------------------------|-----------|-------|------|----------------|
| Russell<br>(2000)[39]   | WS (NS)  | NS                                  | Calbiochem<br>(MS110, Ab-2 and<br>Ab-3)<br>Pharmingen (a.a. 2-<br>20, a.a. 768-793<br>and a.a.1847-1863)<br>(1:100) | 120 min (Room<br>temperature) | Manual                  | Cytoplasm | P     | >10% | 22/51 (43.2%)  |
| Sallum[59]              | TMA (4)  | Citrate buffer,<br>microwave        | Merck Millipore<br>MS110 (1:100)  | Overnight (4)                 | Manual                  | Nucleus   | P + I | ≥5%  | 64/104 (61.5%) |
| Shawky<br>(2014)[40]    | WS (4-5) | NS                                  | Mybiosource Ab-<br>1423 (NS)  | (NS) (NS)                     | Manual                  | Nucleus   | P     | >10% | 13/25 (52.0%)  |
| Shilpa<br>(2014)[41]    | TMA (5)  | Tris EDTA,<br>steam                 | Biocare Medical<br>MS110 (1:50)   | 1h30 (Room<br>temperature)    | Manual                  | Nucleus   | P + I | >10% | 45/64 (70.3%)  |
| Sirisabya<br>(2007)[42] | WS (3)   | Citrate-<br>phosphate,<br>microwave | BioGenex Ab No<br>345P (NS)   | (NS) (NS)                     | Manual                  | Nucleus   | P     | >10% | 87/99 (87.9%)  |
| Skytte<br>(2011)[43]    | WS (3)   | TEG, microwave                      | Merck MS110<br>(1:1000)   | Overnight<br>(Refrigerator)   | Manual and<br>automated | Nucleus   | P     | ≥10% | 18/54 (33.4%)  |

|                          |          |                               |                                       |                              |                         |         |       |      |                 |
|--------------------------|----------|-------------------------------|---------------------------------------|------------------------------|-------------------------|---------|-------|------|-----------------|
| Strickland<br>(2016)[44] | WS (NS)  | EDTA, heat                    | Merck Calbiochem<br>MS110 (1:100)     | 30 min (Room<br>temperature) | Manual                  | Nucleus | P + I | ≥5%  | 1/17 (5.9%)     |
| Sun<br>(2015)[45]        | TMA (4)  | Citric acid, high<br>pressure | Abcam MS110<br>(1:50)                 | (NS) (NS)                    | Manual                  | Nucleus | P + I | Any  | 14/156 (8.9%)   |
| Swisher<br>(2009)[46]    | NS (NS)  | Dako solution,<br>steam heat  | Oncogene MS110<br>(1:250)             | 14-16 h (4)                  | Manual                  | Nucleus | P     | ≥10% | 39/115 (34.0%)  |
| Thrall<br>(2006)[47]     | WS (5)   | Dako solution,<br>steam heat  | Oncotech MS110<br>(1:50)              | 1 h (Room<br>temperature)    | Manual                  | Nucleus | P     | ≥10% | 125/230 (54.4%) |
| Vaz<br>(2007)            | WS (NS)  | Citrate, heat                 | Oncogene MS110<br>(1:300)             | (NS) (NS)                    | Manual                  | Nucleus | P     | >10% | 3/4 (75.0%)     |
| Vorrius<br>(2009)[49]    | TMA (NS) | Heat                          | Merck EMD<br>Calbiochem<br>MS110 (NS) | 60 min (37)                  | Automated               | Nucleus | P + I | >10% | 39/53 (73.6%)   |
| Wang<br>(2004)[50]       | WS (3)   | Citrate, heat                 | Oncogene MS110<br>(NS)                | Overnight (4)                | Manual                  | Nucleus | P + I | ≥10% | 55/76 (72.4%)   |
| Wang L<br>(2015)[52]     | TMA (4)  | Citric acid, high<br>pressure | (NS) MS110 (NS)                       | (NS) (NS)                    | Manual                  | Both    | NS    | NS   | 56/67 (83.6%)   |
| Weberpals<br>(2011)[53]  | TMA (5)  | NS                            | Calbiochem<br>MS110 (1:100)           | 1 h (Room<br>temperature)    | Manual and<br>automated | Nucleus | P + I | Any  | 163/251 (65.0%) |

|                        |          |                                   |  |                           |        |         |       |      |                 |
|------------------------|----------|-----------------------------------|--|---------------------------|--------|---------|-------|------|-----------------|
| Ye<br>(2014)[56]       | WS (4)   | Dako solution,<br>pressure cooker | Merck Anti-<br>BRCA1(1:100)                  | 1 h (Room<br>temperature) | Manual | NS      | P + I | >10% | 29/97 (29.9%)   |
| Zhang<br>(2015)[57]    | TMA (NS) | Microwave                         | Santa Cruz Rabbit<br>anti-BRCA1<br>(1:100)   | 2 h (NS)                  | Manual | Nucleus | P + I | >10% | 57/161 (35.4%)  |
| Zheng<br>(2000)[58]    | WS (5)   | Heat                              | Oncogene MS110<br>(1:200)                    | Overnight (4)             | Manual | Both    | P + I | Any  | 25/38 (65.8%)   |
| <b>BRCA2</b>           |          |                                   |  |                           |        |         |       |      |                 |
| Furukawa<br>(2013)[23] | NS (NS)  | NS                                | R&D Systems<br>Mab2476<br>(NS)               | NS (NS)                   | Manual | NS      | P     | ≥10% | 0/14 (0.0%)     |
| Li<br>(2017)[31]       | TMA (5)  | Citrate, heat                     | Proteintech 19791-<br>1-ap rabbit<br>(1:300) | 14 h (4)                  | Manual | NS      | P + I | Any  | 176/207 (85.0%) |
| Sun<br>(2015)[46]      | TMA (4)  | EDTA                              | R&D Systems<br>Mab2476<br>(1:30)             | NS (NS)                   | Manual | Nucleus | P + I | Any  | 12/156 (7.7%)   |

|                       |          |                              |  |               |           |         |       |      |                 |
|-----------------------|----------|------------------------------|--|---------------|-----------|---------|-------|------|-----------------|
| Swisher<br>(2009)[46] | NS (NS)  | Dako solution,<br>steam heat | Santa Cruz Biotech<br>H-300 rabbit<br>(1:100)      | 14-16 h (4)   | Manual    | Both*   | P     | ≥10% | 49/115 (42.6%)  |
| Vaz<br>(2007)[48]     | WS (NS)  | Citrate, heat                | Calbiochem (ab-2),<br>rabbit IgG<br>(1:100)        | NS (NS)       | Manual    | Nucleus | P     | >10% | 2/4 (50.0%)     |
| Vorrius<br>(2009)[49] | TMA (NS) | Heat                         | Santa Cruz<br>Genetex, Catalog<br>70,121; 3E6 (NS) | 60 min (37)   | Automated | Nucleus | P + I | >10% | 47/54 (87.0%)   |
| Wang Z<br>(2015)[51]  | TMA (5)  | Citrate,<br>microwave        | Santa Cruz<br>Biotechnology<br>Anti-BRCA2<br>(NS)  | NS (NS)       | Manual    | Nucleus | P + I | Any  | 123/150 (82.0%) |
| Yang<br>(2010)[54]    | TMA (5)  | Sodium citrate,<br>microwave | R&D Systems<br>Mab2476<br>(1:200 or 1:100)         | Overnight (4) | Manual    | Nucleus | P     | ≥5%  | 188/223 (84.3%) |
| Yang<br>(2011)[55]    | TMA (5)  | Sodium citrate,<br>microwave | R&D Systems<br>Mab2476<br>(1:200 or 1:100)         | Overnight (4) | Manual    | Nucleus | P     | ≥5%  | 30/51 (58.8%)   |



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|                 |          |           |                              |          |        |         |       |      |                |
|-----------------|----------|-----------|------------------------------|----------|--------|---------|-------|------|----------------|
| Zhang<br>(2015) | TMA (NS) | Microwave | Santa Cruz Rabbit<br>(1:100) | 2 h (NS) | Manual | Nucleus | P + I | >10% | 68/161 (42.2%) |
|-----------------|----------|-----------|------------------------------|----------|--------|---------|-------|------|----------------|

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TMA = tissue microarray; WS = whole-slide; NS = Not specified; \*scored only nuclear staining; P = percentage; I = intensity.