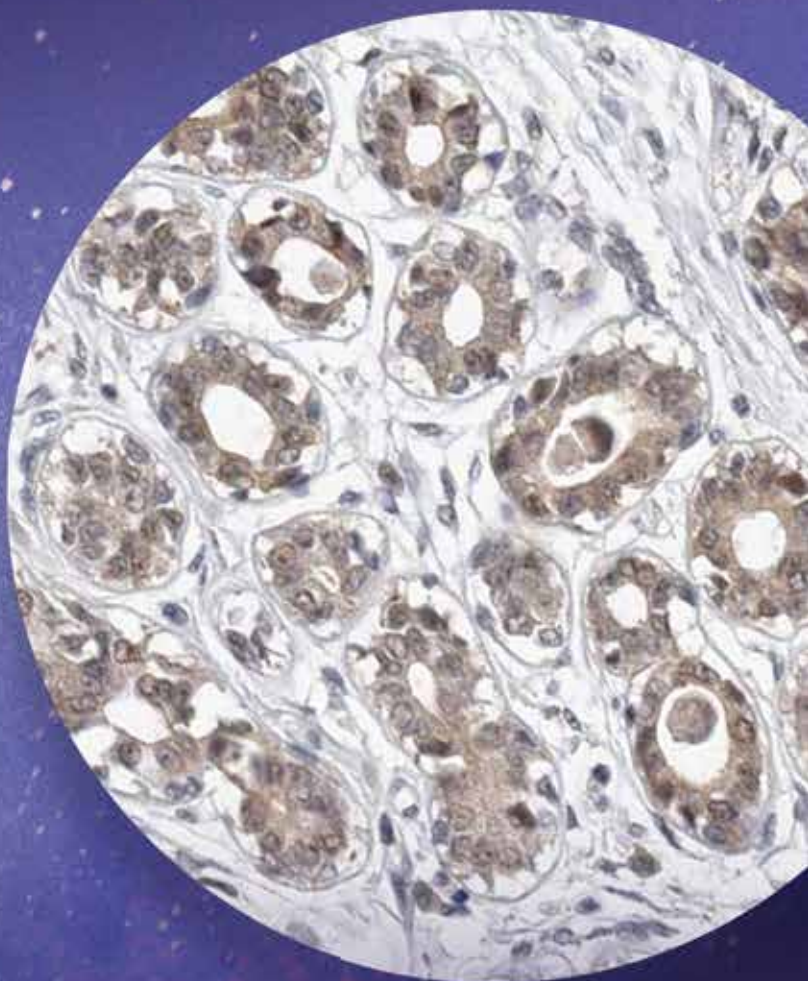
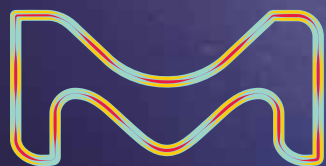
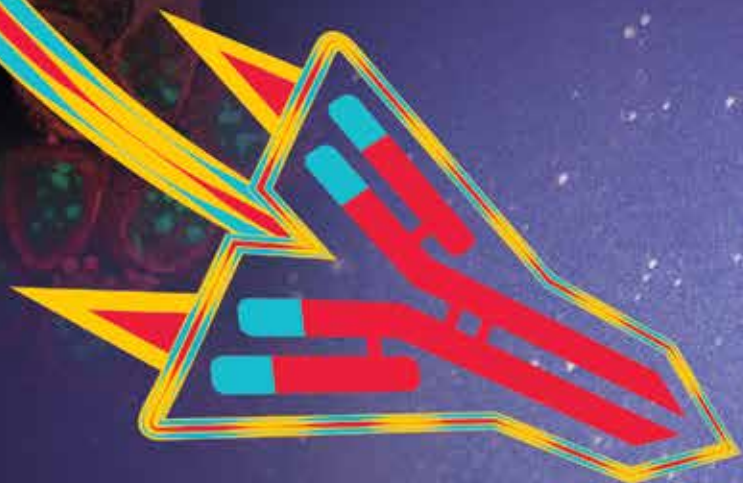


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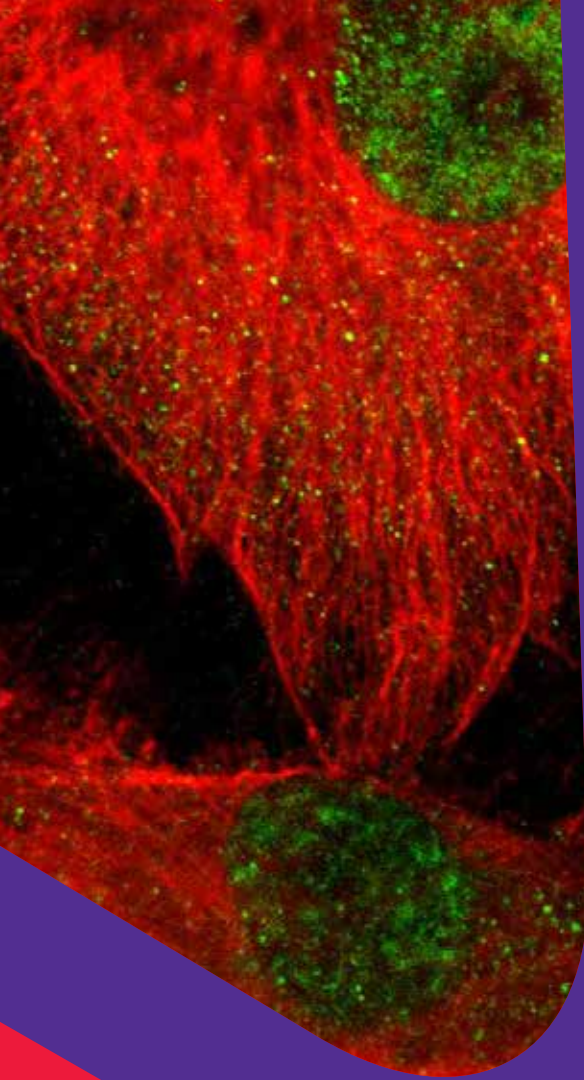
# Prestige Antibodies® Breast Cancer Research

 **ATLAS ANTIBODIES**

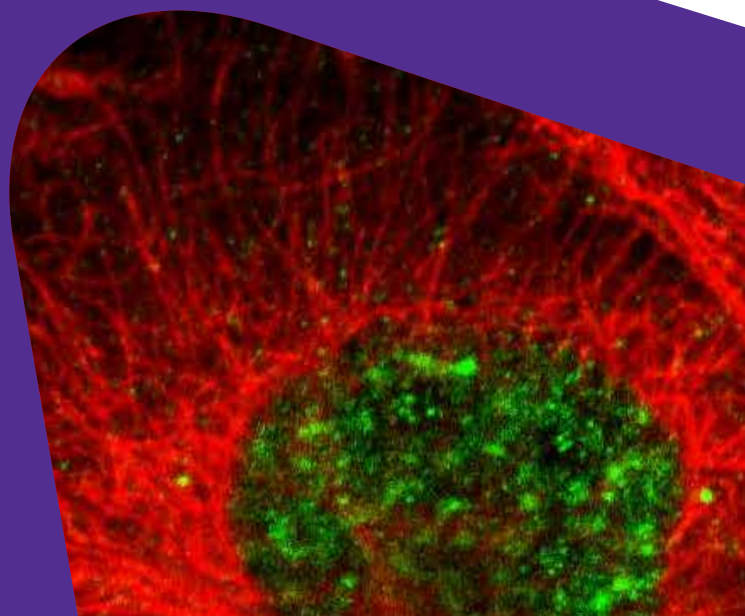


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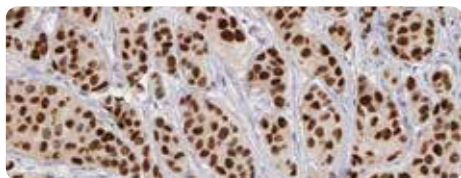


Prestige Antibodies®  
in Breast Cancer  
Research

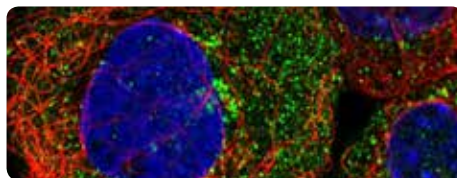


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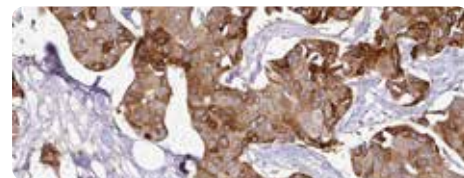
# The Human Protein Atlas



Tissue Atlas



Cell Atlas



Cancer Atlas

## The Human Protein Atlas is Characterizing the Human Proteome

The Human Protein Atlas project has created a complete map of protein expression in all major organs and tissues in the human body<sup>1,2</sup>. To accomplish this, highly specific antibodies have been developed to all protein coding human genes and protein profiling is established in a multitude of tissues and cells using tissue arrays. Applications applied are immunohistochemistry (IHC), Western blot (WB) analysis, protein array assay and immunofluorescent based confocal microscopy (ICC-IF).

The antibodies developed within the Human Protein Atlas project are carefully designed and manufactured to achieve the very highest level of specificity, reproducibility and versatility. You will find them in our catalog as Prestige Polyclonals.

The Human Protein Atlas (HPA) project was initiated in 2003 by Swedish researchers, headed by Professor Mathias Uhlen, and funded by the Knut and Alice Wallenberg foundation. It is a unique world leading effort performing systematic exploration of the human proteome using antibodies.

The Human Protein Atlas is divided into three major parts, the Tissue Atlas, Cell Atlas and Cancer Atlas. In different ways, the atlases show gene and protein expression data and make it easy to access, search and navigate.

## The Tissue Atlas

For all proteins represented in the Tissue Atlas, the expression profiles are based on IHC analysis on a large number of human tissues. All IHC image scan be viewed in high resolution on the Tissue Atlas. The presentation of protein expression data in correlation to RNA sequencing data for each gene is included.

Tissue microarrays containing samples from 44 different normal human tissues and from 20 different cancer types are utilized within the project. The 44 normal tissues are present in triplicate samples and annotated in 76 different cell types. All normal tissue images have undergone pathology-based annotation of expression

levels and are displayed on the normal Tissue Atlas presenting information regarding the expression profiles of human genes both on mRNA and protein level. The mRNA expression data is derived from deep sequencing of RNA (RNASeq) from 37 major different normal tissue types.

## The Cell Atlas

The Cell Atlas presents subcellular localization by confocal microscopy. The results are displayed as high resolution, multicolor images of immunofluorescently stained cells. Three human cell lines for each antibody are selected for the immunofluorescence analysis. Two cell lines from a cell line panel are chosen based on RNA sequencing data and the third cell line is always U-2 OS.

## The Cancer Atlas

The Cancer Atlas contains gene expression data based on protein expression patterns in a multitude of human cancer specimens. Altogether 216 different cancer samples, corresponding to the 20 most common forms of human cancer, have been analyzed for all included genes. All cancer tissue images have been manually annotated by pathologists and just as for the normal Tissue Atlas, protein data includes protein expression levels corresponding to over 15,000 genes for which there are available antibodies.

## Validation in Breast Tissue samples and Cell Lines

IHC images from normal breast samples from three different individuals are available for each antibody in the normal Tissue Atlas. In addition, for each antibody, breast tumor samples from up to 12 patients in duplicates are presented in the Cancer Atlas and for the majority of the antibodies, also images from the MCF-7 and SK-BR-3 breast cell lines in the Cell Line Atlas.

1. Uhlen M et al. (2015) Tissue-based map of the human proteome. *Science* 347(6220):1260-19.

2. Uhlen M et al. (2010) Towards a knowledge-based Human Protein Atlas. *Nat Biotechnol* 28(12):1248-50.

# Prestige Antibodies® Powered by Atlas Antibodies

## Prestige Polyclonals

### **Prestige Polyclonals—the Building Blocks of HPA**

The uniqueness and low cross reactivity of Prestige Polyclonals to other proteins are due to a thorough selection of antigen regions, affinity purification on the recombinant antigen, validation using several methods and a stringent approval process.

The product numbers of Prestige Polyclonals start with “HPA” and of Prestige Monoclonals with “AMAb”.

### **Development**

The Prestige Polyclonals are developed against recombinant human Protein Epitope Signature Tags (PrESTs) of approximately 50 to 150 amino acids. These protein fragments are designed, using a proprietary software, to contain unique epitopes present in the native protein suitable for triggering the generation of antibodies of high specificity. This is achieved by a complete human genome scanning to ensure that PrESTs with the lowest homology to other human proteins are used as antigens.

### **Approval**

The approval of the Prestige Polyclonals relies on a combined validation of the experimental results using IHC, WB or ICC-IF, from RNA sequencing and from information obtained via bioinformatics prediction methods and literature. Since the literature is often inconclusive, an important objective of the HPA project has been to generate paired antibodies with non-overlapping epitopes towards the same protein target, allowing the results and validation of one antibody to be used to validate the other one.

### **Prestige Polyclonal Catalog**

Today, there are more than 17,000 Prestige Polyclonals and new antibodies are added each year.

The antibodies developed and characterized within the Human Protein Atlas project are made available to the scientific community by Atlas Antibodies under the brand name Triple A Polyclonals.

## Prestige Monoclonals

Atlas Antibodies also provide a selected number of mouse monoclonal antibodies, under the brand name Prestige Monoclonals. The Prestige Monoclonal catalog is regularly expanding with new products every year.

### **Unique Features**

Special care is taken in offering clones recognizing only unique non-overlapping epitopes and/or isotypes. Using the same stringent PrEST production process and characterization procedure as for the Triple A Polyclonals, the Prestige Monoclonals offer outstanding performance in approved applications, together with defined specificity, secured continuity and stable supply. In general they also permit high working dilutions and contribute to more standardized assay procedures.

### **Clone Selection**

Functional characterization is performed on a large number of ELISA positive cell supernatants to select the optimal clones for each application prior to subcloning and expansion of selected hybridomas.

### **Epitope Mapping**

Clones are epitope-mapped using synthetic overlapping peptides in a bead-based array format for selection of clones with non-overlapping epitopes only.

### **Isotyping**

All Prestige Monoclonals antibodies are isotyped to allow for multiplexing using isotype-specific secondary antibodies.

### **Hybridoma Cell Cultivation**

Atlas Antibodies use in-vitro methods for the production scale-up phase thus replacing the use of mice for production of ascites fluid.

### **Antibody Characterization**

The characterization of Prestige Monoclonals starts with an extensive literature search to select the most relevant and clinically significant tissues to use for IHC characterization. Often there are more than one tissue type displayed in the IHC application data for each antibody. In addition to positive stained tissue, a negative control tissue staining is also displayed and if relevant, clinical cancer tissue staining.

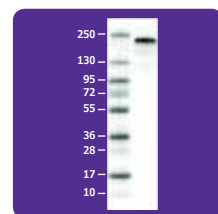
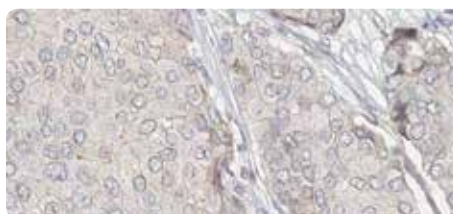
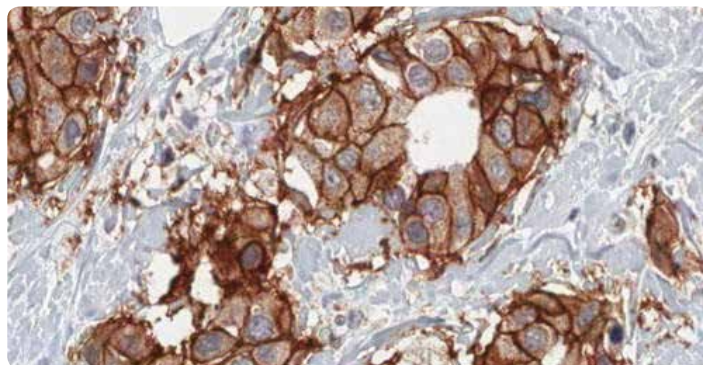
The Western blot (WB) characterization includes results from endogenous human cell or tissue protein lysates or optionally recombinant full-length human protein lysates.

Each Prestige Monoclonal is thus supplied with the most relevant characterization data for its specific target.

# Clinical Markers (ESR1, HER2, Ki67, PGR)

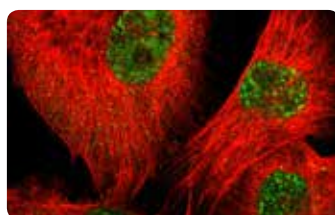
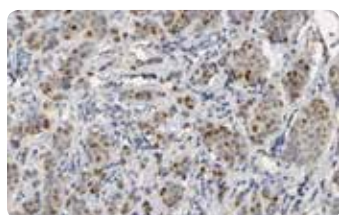
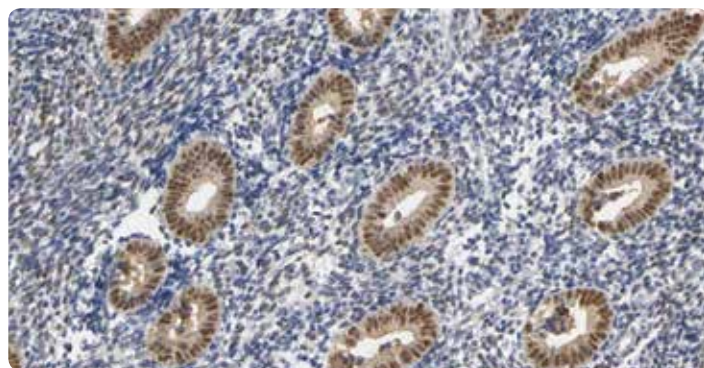
## Established Clinical Breast Cancer Markers

Target Protein	Product Name	Product No.	Validated Applications
Estrogen receptor	Anti-ESR1	HPA000449 <sup>1</sup>	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000450 <sup>1</sup>	IHC,WB
Estrogen receptor	Anti-ESR1	AMAb90867	IHC,WB
Progesteron receptor	Anti-PGR	HPA004751 <sup>2</sup>	IHC
Progesteron receptor	Anti-PGR	HPA008428 <sup>3</sup>	IHC
Progesteron receptor	Anti-PGR	HPA017176	IHC
HER2/ERBB2	Anti-ERBB2	HPA001383 <sup>3,4</sup>	IHC,WB,ICC-IF
HER2/ERBB2	Anti-HER2	AMAb90627	IHC,WB
Ki67/MKI67	Anti-MKI67	HPA000451 <sup>5,6</sup>	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	HPA001164 <sup>7</sup>	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	AMAb90870	IHC



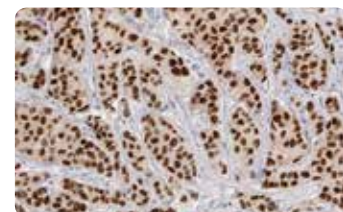
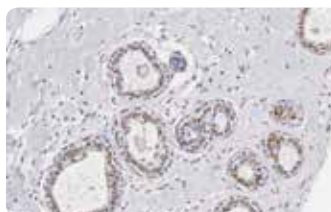
### HER2/ERBB2

Immunohistochemical staining of human breast tumour using Anti-HER2 (AMAb90627) shows strong membranous (combined with moderate cytoplasmic) positivity in tumour cells in HER2-positive ductal carcinoma, while HER2-negative ductal carcinoma shows no membranous positivity. By Western Blot analysis, HER2 is detected in the breast cancer cell line SK-BR-3.



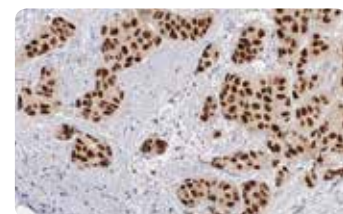
### Progesteron receptor

IHC staining using the Anti-PGR antibody (HPA004751) in normal human corpus (uterine) tissue shows strong nuclear positivity in glandular cells. In the presented breast cancer sample, the staining of tumor cells is also nuclear. ICC-IF shows nuclear staining in U-251MG cells (in green).



### Estrogen receptor

The Anti-ESR1 antibody (HPA000449) shows distinct nuclear positivity in glandular cells in human breast tissue and in tumor cells in breast cancer samples using IHC.

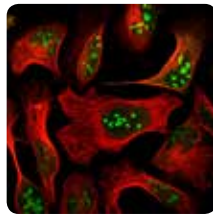
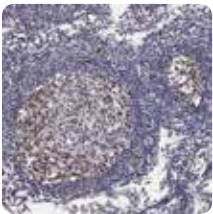


IHC staining using the Anti-ESR1 antibody (HPA000450) shows strong nuclear positivity in glandular and stromal cells of human corpus, uterine tissue and in tumor cells in breast cancer.

1. Algenäs C et al. Antibody performance in western blot applications is context-dependent. *Biotechnol J* 2014 Mar; 9(3):435-45. Epub 2014 Jan 29.
2. Pereira CB et al. Prognostic and Predictive Significance of MYC and KRAS Alterations in Breast Cancer from Women Treated with Neoadjuvant Chemotherapy. *PLoS One* 2013;8(3):e60576.
3. Huvila J et al. Progesterone receptor negativity is an independent risk factor for relapse in patients with early stage endometrioid endometrial adenocarcinoma. *Gynecol Oncol* 2013 Sep; 130(3):463-9. Epub 2013 Jun 15.
4. Newie I et al. The HER2-Encoded miR-4728-3p Regulates ESR1 through a Non-Canonical Internal Seed Interaction. *PLoS One* 2014; 9(5):e97200. Epub 2014 May 14.
5. Li S et al. Endothelial VEGF Sculpts Cortical Cytoarchitecture. *J Neurosci* 2013 Sep 11; 33(37):14809-14815.

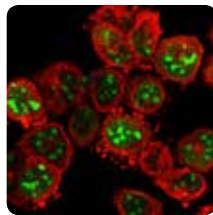
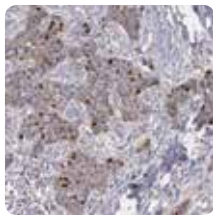
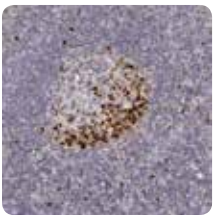
6. Pohler E et al. Haploinsufficiency for AAGAB causes clinically heterogeneous forms of punctate palmoplantar keratoderma. *Nat Genet.* 2012 Nov; 44(11):10.1038/ng.2444. Epub 2012 Oct 14.

7. Roca H et al. IL-4 induces proliferation in prostate cancer PC3 cells under nutrient-depletion stress through the activation of the JNK-pathway and survivin upregulation. *J Cell Biochem* 2012 May; 113(5):1569-1580.

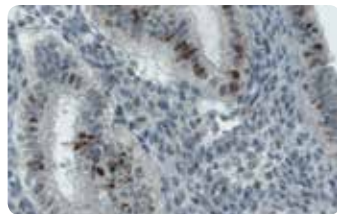
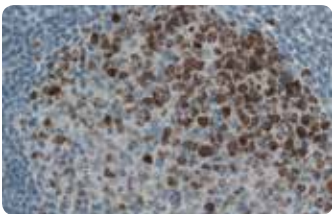


### Ki67

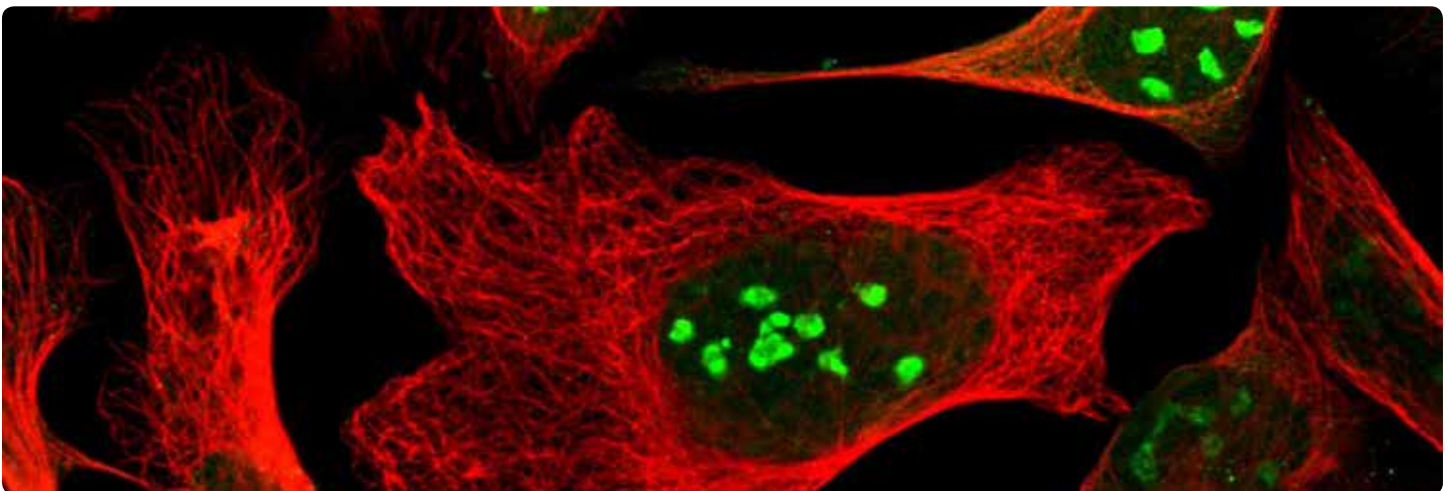
The Anti-MKI67 antibody (HPA000451) shows strong nuclear positivity in a fraction of cells in the reaction center in human lymph node using IHC. In breast cancer, the staining of tumor cells is also nuclear and by ICC-IF, staining of the human cell line U-2OS shows positivity in nucleoli (in green).



IHC staining of human tonsil tissue using the Anti-MKI67 antibody (HPA001164) shows nuclear staining of reaction center cells. In tumor cells in breast cancer, the staining is mainly nuclear and in U-2OS cells, using t, nucleoli show strong positivity (green).



IHC staining of lymph node in human colon shows strong nuclear and nucleolar immunoreactivity in the reaction center cells using the monoclonal Anti-MKI67 antibody (AMAb90870). In uterus, nuclear positivity in a subset of glandular cells is shown.

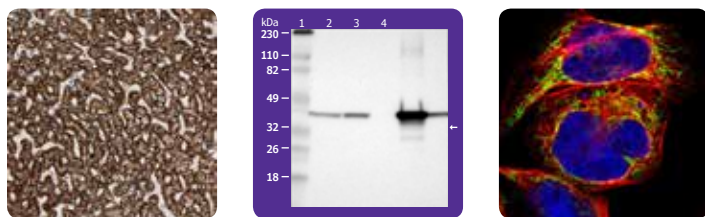


## Antibodies used in Breast Cancer Research

In this section, antibodies are selected either on a reference/article-basis or on breast cancer relevance for the corresponding target protein.

Target Protein	Proudct Name	Product No.	Validated Applications
53BP1	Anti-TP53BP1	HPA008788	IHC,ICC-IF
53BP1	Anti-TP53BP1	HPA022133	IHC,W-B*,ICC-IF
ACAT1	Anti-ACAT1	HPA004428 <sup>1</sup>	IHC,W-B*,ICC-IF
ACAT1	Anti-ACAT1	HPA007569 <sup>2-4</sup>	IHC,WB,ICC-IF
ADAM2/CT15/PH30	Anti-ADAM2	HPA026581 <sup>5</sup>	IHC
AGR2	Anti-AGR2	HPA007912 <sup>6</sup>	IHC,WB
AIB1/NCOA3	Anti-NCOA3	HPA024210 <sup>7</sup>	IHC,WB,ICC-IF
AKAP1/PRKA1	Anti-AKAP1	HPA008691 <sup>8</sup> HPA008691	IHC,WB,ICC-IF
AKT3/PKB gamma	Anti-AKT3	HPA026441 <sup>9,10</sup>	IHC,WB,ICC-IF
AMOTL1	Anti-AMOTL1	HPA001196 <sup>11</sup>	IHC,WB
Amphiregulin	Anti-AREG	HPA008720 <sup>12</sup>	IHC
ANAPC15/C11orf51	Anti-ANAPC15	HPA036596	IHC,WB,ICC-IF
Anillin/ANLN	Anti-ANLN	AMAb90660	IHC,WB
Anillin/ANLN	Anti-ANLN	AMAb90662	IHC,WB,ICC-IF
Anillin/ANLN	Anti-ANLN	HPA005680 <sup>13,14</sup>	IHC,WB,ICC-IF
ARG1	Anti-ARG1	HPA024006 <sup>15-17</sup>	IHC
ARG1	Anti-ARG1	AMAb90545	IHC,WB
ASAH1	Anti-ASAH1	HPA005468 <sup>18-22</sup>	IHC,WB
BAAT1/BRAT1	Anti-BRAT1	HPA029455	IHC,WB
BAP1	Anti-BAP1	HPA028814	IHC,WB
BARD1	Anti-BARD1	HPA044864	IHC,ICC-IF
Beta-Catenin	Anti-CTNNB1	HPA029159	IHC,W-B*,ICC-IF
Beta-Catenin	Anti-CTNNB1	HPA029160	IHC,ICC-IF
Beta-Catenin	Anti-CTNNB1	AMAb91210	IHC,WB
BIRC3/API2	Anti-BIRC3	HPA002317 <sup>23-25</sup>	IHC,WB,ICC-IF

\* WB both in human and rodent samples

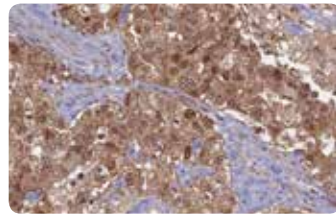
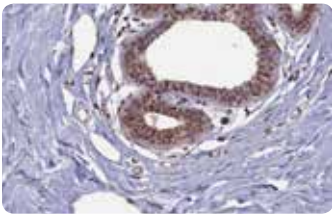


### ACAT1

Immunohistochemical staining of human liver tissue using Anti-ACAT1 (HPA004428) shows strong cytoplasmic positivity in hepatocytes. By Western Blot analysis, ACAT1 is detected in the human cell lines RT-4 and U251-MG and in liver and tonsil tissue lysates. By ICC-IF in the human cell line A-431, positivity is shown in mitochondria (in green).

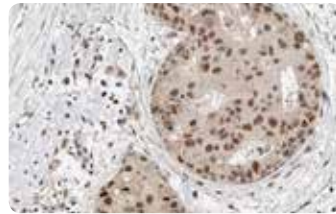
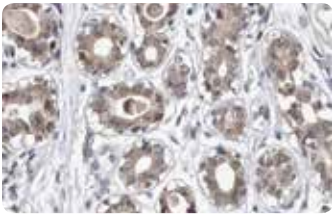
- Sanchez-Alvarez R et al. Ethanol exposure induces the cancer-associated fibroblast phenotype and lethal tumor metabolism: Implications for breast cancer prevention. *Cell Cycle* 2013 Jan 15; 12(2):289-301.
- Martinez-Outschoorn UE et al. Ketone bodies and two-compartment tumor metabolism: Stromal ketone production fuels mitochondrial biogenesis in epithelial cancer cells. *Cell Cycle* 2012 Nov 1; 11(21):3956-3963.
- Martinez-Outschoorn UE et al. Ketone body utilization drives tumor growth and metastasis. *Cell Cycle* 2012 Nov 1;11(21):3964-71.
- Chang HT et al. Ketolytic and glycolytic enzymatic expression profiles in malignant gliomas: implication for ketogenic diet therapy. *Nutr Metab (Lond)* 1047. Epub 2013/07/05.
- Maheswaran E et al. Lack of ADAM2, CALR3 and SAGE1 Cancer/Testis Antigen Expression in Lung and Breast Cancer. *PLoS One* 2015; 10(8):e0134967. Epub 2015 Aug 7.
- Hrstka R et al. AGR2 Predicts Tamoxifen Resistance in Postmenopausal Breast Cancer Patients. *Dis Markers* 2013; 35(4):207-212. Epub 2013/09/03.
- Battistella M et al. The High Expression of the microRNA 17-92 Cluster and its Paralog, and the Downregulation of the Target Gene PTEN, Is Associated with Primary Cutaneous B-Cell Lymphoma Progression. *Journal of Investigative Dermatology* January 29, 2015.
- Sotgia F et al. Mitochondria "fuel" breast cancer metabolism: Fifteen markers of mitochondrial biogenesis label epithelial cancer cells, but are excluded from adjacent stromal cells. *Cell Cycle* 2012 Dec 1; 11(23):4390-4401.
- O'Hurley G et al. Investigation of molecular alterations of AKT-3 in triple-negative breast cancer. *Histopathology* 2014 Apr; 64(5):660-70. Epub 2013 Dec 12.
- Vredevelde LC et al. Abrogation of BRAFV600E-induced senescence by PI3K pathway activation contributes to melanomagenesis. *Genes Dev* 2012 May 15; 26(10):1055-1069.
- Couderc C et al. AMOTL1 Promotes Breast Cancer Progression and Is Antagonized by Merlin. *Neoplasia* 2016 Jan; 18(1):10-24. Epub 2016 Jan 21.
- Barton VN et al. Multiple Molecular Subtypes of Triple-Negative Breast Cancer Critically Rely on Androgen Receptor and Respond to Enzalutamide In Vivo. *Mol Cancer Ther* 2015 Mar; 14(3):769-778. Epub 2015 Feb 23.
- O'Leary PC et al. Systematic antibody generation and validation via tissue microarray technology leading to identification of a novel protein prognostic panel in breast cancer. *BMC Cancer*. 2013 Apr 2;13:175.
- Hjelm B et al. Generation of monospecific antibodies based on affinity capture of polyclonal antibodies. *Protein Sci*. 2011 Nov; 20(11):1824-35. Epub 2011 Oct 12.
- de Boniface J et al. Expression patterns of the immunomodulatory enzyme arginase 1 in blood, lymph nodes and tumor tissue of early-stage breast cancer patients. *Oncoimmunology* 2012 Nov 1; 1(8):1305-1312.
- Hashimoto-Kataoka T et al. Interleukin-6/interleukin-21 signaling axis is critical in the pathogenesis of pulmonary arterial hypertension. *Proc Natl Acad Sci U S A* 2015 May 19; 112(20):E2677-E2686. Epub 2015 May 4.
- Geiger T et al. Initial Quantitative Proteomic Map of 28 Mouse Tissues Using the SILAC Mouse. *Mol Cell Proteomics* 2013 Jun; 12(6):1709-1722. Epub 2013 Feb 22.
- Lucki NC et al. Acid Ceramidase (ASAH1) Represses Steroidogenic Factor 1-Dependent Gene Transcription in H295R Human Adrenocortical Cells by Binding to the Receptor. *Mol Cell Biol* 2012 Nov; 32(21):4419-4431.
- Cai K et al. Silencing diacylglycerol kinase-theta expression reduces steroid hormone biosynthesis and cholesterol metabolism in human adrenocortical cells. *Biochim Biophys Acta* 2014 Apr 4; 1841(4):552-562. Epub 2013 Dec 22.
- Lucki NC et al. Acid Ceramidase (ASAH1) Is a Global Regulator of Steroidogenic Capacity and Adrenocortical Gene Expression. *Mol Endocrinol* 2012 Feb; 26(2):228-243. Epub 2012 Jan 19.
- Lucki NC and Sewer MB. Genistein Stimulates MCF-7 Breast Cancer Cell Growth by Inducing Acid Ceramidase (ASAH1) Gene Expression. *J Biol Chem* 2011 Jun 3; 286(22):19399-19409. Epub 2011 Apr 14.
- Lucki NC and Sewer MB. Athe cAMP-responsive element binding protein (CREB) regulates the expression of acid ceramidase (ASAH1) in H295R human adrenocortical cells. *Biochim Biophys Acta* 2009 Aug; 1791(8):706-713. Epub 2009 Mar 16.
- Jones DR et al. APhase I Trial of Induction Histone Deacetylase and Proteasome Inhibition Followed by Surgery in Non-small Cell Lung Cancer. *J Thorac Oncol* 2012 Nov; 7(11):1683-1690.
- Almubarak H et al. Zoledronic acid directly suppresses cell proliferation and induces apoptosis in highly tumorigenic prostate and breast cancers. *J Carcinog* 2011 Jan 15; 10:2. Epub 2011 Jan 15.
- Mulder J et al. Tissue Profiling of the Mammalian Central Nervous System Using Human Antibody-based Proteomics. *Mol Cell Proteomics* 2009 Jul; 8(7):1612-1622. Epub 2009 Apr 7.





### BRCA1

The Anti-BRCA1 antibody (HPA034966) shows positivity in glandular cells in normal human breast tissue and in tumor cells in breast cancer samples using IHC.



### BRCA2

IHC staining using the Anti-BRCA2 antibody (HPA026815) in normal human breast tissue shows positivity in glandular cells. In breast cancer, nuclear staining of tumor cells is shown.

26. Brunquell C *et al.* TLE1 is an anoikis regulator and is downregulated by Bit1 in breast cancer cells. *Mol Cancer Res* 2012 Nov; 10(11):1482-1495. Epub 2012/09/04.

27. Karmali PP *et al.* Metastasis of tumor cells is enhanced by downregulation of bit1. *PLoS One* 2011;6(8):e23840.

28. Yao X *et al.* The Anoikis Effector Bit1 Displays Tumor Suppressive Function in Lung Cancer Cells. *PLoS One* 2014; 9(7):e101564. Epub 2014 Jul 8.

29. Meena JK *et al.* Telomerase abrogates aneuploidy-induced telomere replication stress, senescence and cell depletion. *EMBO J* 2015 May 12; 34(10):1371-1384. Epub 2015 Mar 27.

30. Lao VV *et al.* Altered RECQ Helicase Expression in Sporadic Primary Colorectal Cancers. *Transl Oncol* 2013 Aug; 6(4):458-469. Epub 2013 Aug 1.

31. Chiang SC *et al.* Prioritization of Cancer Marker Candidates Based on the Immunohistochemistry Staining Images Deposited in the Human Protein Atlas. *PLoS One* 2013; 8(11):e81079. Epub 2013 Nov 26.

32. Zou W *et al.* BRIP1 inhibits the tumorigenic properties of cervical cancer by regulating RhoA GTPase activity. *Oncol Lett* 2016/01/01; 11(1):551-558. Epub 2015 Nov 24.

33. Vermeulen JF *et al.* Immunophenotyping invasive breast cancer: paving the road for molecular imaging. *BMC Cancer* 12240. Epub 2012 Jun 13.

34. Davidson B *et al.* Gene expression signatures differentiate ovarian/peritoneal serous carcinoma from breast carcinoma in effusions. *J Cell Mol Med* 2011 Mar;15(3):535-44.

35. Vermeulen JF *et al.* Differential expression of growth factor receptors and membrane-bound tumor markers for imaging in male and female breast cancer. *PLoS One* 2013;8(1):e53353.

36. Tafreshi NK *et al.* Noninvasive detection of breast cancer lymph node metastasis using carbonic anhydrases IX and XII targeted imaging probes. *Clin Cancer Res* 2012 Jan 1;18(1):207-19.

37. Vazquez-Martin A *et al.* Metformin regulates breast cancer stem cell ontogeny by transcriptional regulation of the epithelial-mesenchymal transition (EMT) status. *Cell Cycle* 2010 Sep 15;9(18):3807-14.

38. Baccelli I *et al.* Identification of a population of blood circulating tumor cells from breast cancer patients that initiates metastasis in a xenograft assay. *Nat Biotechnol* 2013 Apr 21;

39. Petit V *et al.* Optimization of tumor xenograft dissociation for the profiling of cell surface markers and nutrient transporters. *Lab Invest* 2013 May;93(5):611-21.

40. Twarock S *et al.* Synthesis of hyaluronan in oesophageal cancer cells is uncoupled from the prostaglandin-cAMP pathway. *Br J Pharmacol* 2009 May;157(2):234-43.

41. Asplund A *et al.* Expression profiling of microdissected cell populations selected from basal cells in normal epidermis and basal cell carcinoma. *Br J Dermatol* 2008 Mar;158(3):527-38.

Target Protein	Product Name	Product No.	Validated Applications
BIT1/ PTRH2	Anti-PTRH2	HPA012897 <sup>26-28</sup>	IHC,WB,ICC-IF
Blooms Syndrome Prot	Anti-BLM	HPA005689 <sup>29-30</sup>	IHC,ICC-IF
Bmi1	Anti-BMI1	HPA030472	IHC,WB*
BRCA1	Anti-BRCA1	HPA034966 <sup>31</sup>	IHC,ICC-IF
BRCA2	Anti-BRCA2	HPA026815	IHC,ICC-IF
BRIP1/FANCI	Anti-BRIP1	HPA005474 <sup>32</sup>	IHC,WB,ICC-IF
CASP8	Anti-CASP8	HPA001302	IHC,WB,ICC-IF
CASP8	Anti-CASP8	HPA005688	IHC,WB,ICC-IF
CAXII/CA12	Anti-CA12	HPA008773 <sup>33-36</sup>	IHC,WB
CAXII/CA12	Anti-CA12	AMAb90639	IHC,WB
CD44	Anti-CD44	HPA005785 <sup>37-43</sup>	IHC,WB,ICC-IF
CD82	Anti-CD82	HPA028900	IHC,WB
CDH1	Anti-CDH1	AMAb90863	IHC,WB
CDH1	Anti-CDH1	HPA004812	IHC,ICC-IF
CEA/CEACAM5	Anti-CEACAM5	HPA019758	IHC,WB
CHEK2	Anti-CHEK2	HPA001878	IHC,WB,ICC-IF
CKB	Anti-CKB	HPA001254 <sup>44,45</sup>	IHC,ICC-IF
CRABP2	Anti-CRABP2	HPA004135 <sup>46</sup>	IHC,WB,ICC-IF
CT83/KK-LC-1	Anti-CT83	HPA004773 <sup>47</sup>	IHC
CTNND1	Anti-CTNND1	HPA015955	IHC,WB*,ICC-IF
Cyclin E1	Anti-CCNE1	HPA018169 <sup>48</sup>	IHC,ICC-IF
cyklin A2	Anti-CCNA2	HPA020626	IHC,WB
Cytokeratin 14/CK14	Anti-KRT14	HPA023040	IHC
Cytokeratin 17/CK17	Anti-KRT17	HPA000452 <sup>49</sup>	IHC,WB
Cytokeratin 17/CK17	Anti-KRT17	HPA000453	IHC,WB

\* WB both in human and rodent samples

42. Ma R *et al.* Superficial scrapings from breast tumors is a source for biobanking and research purposes. *Laboratory Investigation* 2014 94, 796-805.

43. Schneck H *et al.* EpCAM-Independent Enrichment of Circulating Tumor Cells in Metastatic Breast Cancer. *PLoS One* 1/01/01; 10(12):e0144535. Epub 2015 Dec 22.

44. Mello AA *et al.* Deregulated Expression of SRC, LYN and CKB Kinases by DNA Methylation and Its Potential Role in Gastric Cancer Invasiveness and Metastasis. *PLoS One* 2015; 10(10):e0140492. Epub 2015 Oct 13.

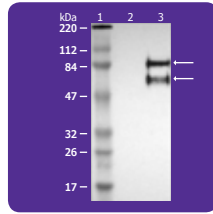
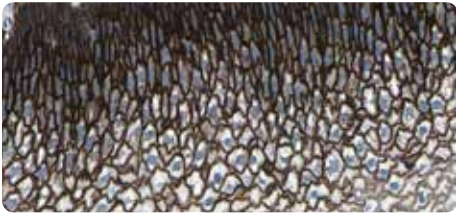
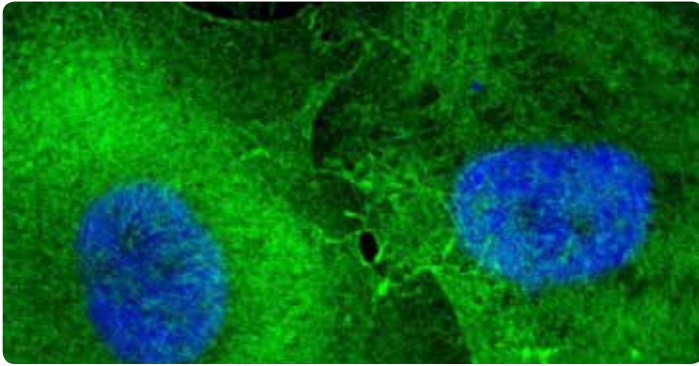
45. Bachmann J *et al.* Affinity Proteomics Reveals Elevated Muscle Proteins in Plasma of Children with Cerebral Malaria. *PLoS Pathog* 2014 Apr; 10(4):e1004038. Epub 2014 Apr 17.

46. Seidensaal K *et al.* Impaired aldehyde dehydrogenase 1 subfamily member 2A-dependent retinoic acid signaling is related with a mesenchymal-like phenotype and an unfavorable prognosis of head and neck squamous cell carcinoma. *Mol Cancer* 2015/12/03; 14:204. Epub 2015 Dec 3.

47. Paret C *et al.* CXorf61 is a target for T cell based immunotherapy of triple-negative breast cancer. *Oncotarget* 2015 Sep 22; 6(28):25356-25367. Epub 2015 Jul 29.

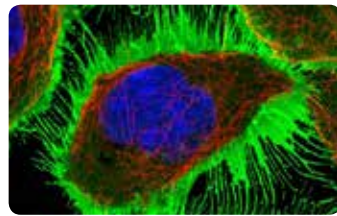
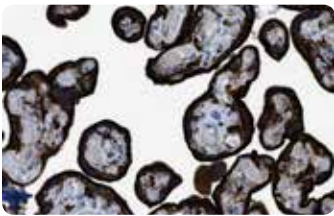
48. Fu YP *et al.* The 19q12 bladder cancer GWAS signal: association with cyclin E function and aggressive disease. *Cancer Res* 2014 Oct 15; 74(20):5808-5818.

49. Kiflemariam S *et al.* Scalable in situ hybridization on tissue arrays for validation of novel cancer and tissue-specific biomarkers. *PLoS One* 2012;7(3):e32927.



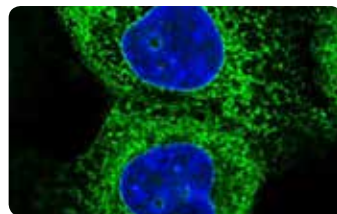
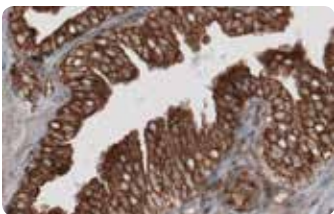
**CD44**

Immunohistochemical staining of human esophagus tissue using Anti-CD44 (HPA005785) shows strong cytoplasmic and membranous positivity in squamous epithelial cells. By Western Blot analysis, CD44 is detected in the human cell line U-251MG. ICC-IF in the human cell line U-251MG shows positivity in plasma membrane in green.



**EGFR**

IHC staining using the Anti-EGFR antibody (HPA018530) in normal human placenta tissue shows strong positivity in trophoblasts. Using ICC-IF in human cell line A-431, strong staining of plasma membrane is shown in green.



**Endoplasmin**

IHC staining using the Anti-HSP90B1 antibody (AMAb91019) in normal human prostate shows strong cytoplasmic positivity in glandular cells. Using ICC-IF in human cell line A-431, strong positivity in endoplasmic reticulum is shown (in green).

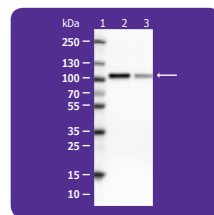
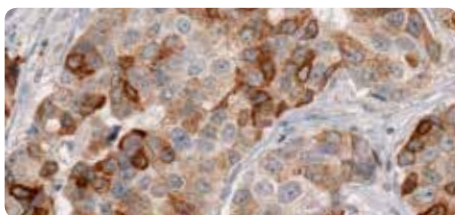
50. Nodin B *et al.* Discovery of dachshund 2 protein as a novel biomarker of poor prognosis in epithelial ovarian cancer. *J Ovarian Res* 2012 Jan 27;5(1):6.  
 51. Sircoulomb F *et al.* ZNF703 gene amplification at 8p12 specifies luminal B breast cancer. *EMBO Mol Med* 2011 Mar; 3(3):153-166. Epub 2011 Feb 15.  
 52. Abdel-Fatah TM *et al.* HAGE (DDX43) is a biomarker for poor prognosis and a predictor of chemotherapy response in breast cancer. *Br J Cancer* 2014 May 13; 110(10):2450-2461. Epub 2014 Apr 22.  
 53. Henke A *et al.* Stromal Expression of Decorin, Semaphorin6D, SPARC, Sprouty1 and Tsukushi in Developing Prostate and Decreased Levels of Decorin in Prostate Cancer. *LoS One* 7(8):e42516. Epub 2012 Aug 3.  
 54. Cawthorn TR *et al.* Proteomic Analyses Reveal High Expression of Decorin and Endoplasmin (HSP90B1) Are Associated with Breast Cancer Metastasis and Decreased Survival. *PLoS One* 2012;7(2):e30992.  
 55. Bozoky B *et al.* Decreased decorin expression in the tumor microenvironment. *Cancer Med* 2014 Jun; 3(3):485-491. Epub 2014 Mar 17.  
 56. Edlund K *et al.* CD99 is a novel prognostic stromal marker in non-small cell lung cancer. *Int J Cancer* 2012 Nov 15; 131(10):2264-73. Epub 2012 Apr 24.  
 57. Montanaro L *et al.* Relationship between dyskerin expression and telomerase activity in human breast cancer. *Cell Oncol* 2008; 30(6):483-90.  
 58. Koskimaa HM *et al.* Molecular markers implicating early malignant events in cervical carcinogenesis. *Cancer Epidemiol Biomarkers Prev* 2010 Aug; 19(8):2003-12. Epub 2010 Jul 20.

Target Protein	Product Name	Product No.	Validated Applications
DACH2	Anti-DACH2	HPA000258 <sup>50</sup>	IHC
DBC1/KIAA1967	Anti-KIAA1967	HPA019907	IHC,WB*,ICC-IF
DBC1/KIAA1967	Anti-KIAA1967	HPA019943	IHC
DCAF7	Anti-DCAF7	HPA022962 <sup>51</sup>	IHC,WB
DDX43/CT13	Anti-DDX43	HPA031381 <sup>52</sup>	IHC,WB,ICC-IF
Decorin/DCN	Anti-DCN	HPA003315 <sup>53-56</sup>	IHC,WB
DIRAS3	Anti-DIRAS3	HPA028483	IHC,WB
DIRAS3	Anti-DIRAS3	HPA028557	IHC,WB
DIRAS3	Anti-DIRAS3	HPA029384	IHC,ICC-IF
DKC1	Anti-DKC1	HPA000166 <sup>57-59</sup>	IHC,WB,ICC-IF
DOCK8	Anti-DOCK8	HPA003218 <sup>60-61</sup>	IHC,WB
EGFR	Anti-EGFR	AMAb90816	IHC,WB
EGFR	Anti-EGFR	AMAb90819	WB
EGFR	Anti-EGFR	HPA001200 <sup>62</sup>	IHC
EGFR	Anti-EGFR	HPA018530 <sup>63,64</sup>	IHC,WB,ICC-IF
Endoplasmin/HSP90B1	Anti-HSP90B1	HPA003901 <sup>54,65</sup>	IHC,WB,ICC-IF
Endoplasmin/HSP90B1	Anti-HSP90B1	AMAb91019	IHC,WB,ICC-IF
EPSTI1	Anti-EPSTI1	HPA017362 <sup>66</sup>	IHC,WB,ICC-IF
ERLIN2	Anti-ERLIN2	HPA002025 <sup>67,68</sup>	IHC,WB*,ICC-IF
ERFF/C1orf64	Anti-C1orf64	HPA026676 <sup>69</sup>	IHC,WB
FAAH	Anti-FAAH	HPA007425 <sup>70</sup>	IHC
FGFR2	Anti-FGRF2	HPA035305 <sup>71</sup>	IHC,WB
G3BP-2	Anti-G3BP2	HPA018304 <sup>72</sup>	IHC,WB,ICC-IF
GATA3	Anti-GATA3	HPA029731	IHC,WB
GGH	Anti-GGH	HPA025226 <sup>70</sup>	IHC,WB
GOLPH3/MIDAS	Anti-GOLPH3	HPA044564 <sup>8</sup>	IHC
GOLPH3L	Anti-GOLPH3L	HPA028558 <sup>8</sup>	IHC,WB,ICC-IF
GP2	Anti-GP2	HPA016668 <sup>73</sup>	IHC
GPAT2	Anti-GPAT2	HPA036841 <sup>74,75</sup>	IHC

\* WB both in human and rodent samples

59. Sieron P *et al.* DKC1 overexpression associated with prostate cancer progression. *Br J Cancer* 2009 Oct 20; 101(8):1410-6. Epub 2009 Sep 15.
60. Johansson J *et al.* TGF- $\beta$ 1-Induced Epithelial-Mesenchymal Transition Promotes Monocyte/Macrophage Properties in Breast Cancer Cells. *Front Oncol* 2015; 5:3. Epub 2015 Jan 26.
61. Jabara HH *et al.* DOCK8 functions as an adaptor that links TLR-MyD88 signaling to B cell activation. *Nat Immunol* 2012 May 13; 13(6):612-20. Epub 2012 May 13.
62. Hudson EP *et al.* Multiplex epitope mapping using bacterial surface display reveals both linear and conformational epitopes. *Sci Rep* 2012;2:706.
63. Arabi A *et al.* Proteomic screen reveals Fbw7 as a modulator of the NF- $\kappa$ B pathway. *Nat Commun* 2012;3:976.
64. Luke GP *et al.* Sentinel lymph node biopsy revisited: ultrasound-guided photoacoustic detection of micrometastases using molecularly targeted plasmonic nanosensors. *Cancer Res* 2014 Oct 1; 74(19):5397-5408. Epub 2014 Aug 8.
65. Ito A *et al.* Novel application for pseudopodia proteomics using excimer laser ablation and two-dimensional difference gel electrophoresis. *Lab Invest* 2012 Sep;92(9):1374-85.
66. Li T *et al.* Identification of epithelial stromal interaction 1 as a novel effector downstream of Kruppel-like factor 8 in breast cancer invasion and metastasis. *Oncogene* 2014 Sep 25; 33(39):4746-4755. Epub 2013 Oct 7.
67. Holland DG *et al.* ZNF703 is a common Luminal B breast cancer oncogene that differentially regulates luminal and basal progenitors in human mammary epithelium. *EMBO Mol Med* 2011 Mar;3(3):167-80.
68. Mulder J *et al.* Tissue profiling of the mammalian central nervous system using human antibody-based proteomics. *Mol Cell Proteomics* 2009 Jul;8(7):1612-22.
69. Su D *et al.* Role of ERF, a Novel ER-Related Nuclear Factor, in the Growth Control of ER-Positive Human Breast Cancer Cells. *Am J Pathol* 2012 Mar; 180(3):1189-1201.
70. Shubbar E *et al.* High levels of  $\gamma$ -glutamyl hydrolase (GGH) are associated with poor prognosis and unfavorable clinical outcomes in invasive breast cancer. *BMC Cancer* 2013 Feb 1;13:47.
71. Tchaicha JH *et al.* Kinase domain activation of FGFR2 yields high-grade lung adenocarcinoma sensitive to a pan-FGFR inhibitor in a mouse model of NSCLC. *Cancer Res* 2013 Feb 1;13:47.
72. Katz E *et al.* Targeting of Rac GTPases blocks the spread of intact human breast cancer. *Oncotarget* 2012 Jun; 3(6):608-619. Epub 2012 Jun 9.
73. Muraoka S *et al.* Strategy for SRM-based verification of biomarker candidates discovered by iTRAQ method in limited breast cancer tissue samples. *J Proteome Res* 2012 Aug 3; 11(8):4201-10. Epub 2012 Jul 9.
74. Pellon-Maison M *et al.* Glycerol-3-Phosphate Acyltransferase-2 Behaves as a Cancer Testis Gene and Promotes Growth and Tumorigenicity of the Breast Cancer MDA-MB-231 Cell Line. *PLoS One* 2014; 9(6):e100896. Epub 2014 Jun 26.
75. Cattaneo ER *et al.* Glycerol-3-Phosphate Acyltransferase-2 Is Expressed in Spermatid Germ Cells and Incorporates Arachidonic Acid into Triacylglycerols. *PLoS One* 2012; 7(8):e42986. Epub 2012 Aug 8.
76. Elkabets M *et al.* Human tumors instigate granulins-expressing hematopoietic cells that promote malignancy by activating stromal fibroblasts in mice. *J Clin Invest* 2011 Feb 1;121(2):784-99.
77. Ruckhäberle E *et al.* Breast Cancer Proteomics – Differences in Protein Expression between Estrogen Receptor-Positive and -Negative Tumors Identified by Tandem Mass Tag Technology. *Breast Care (Basel)* 2010 Mar; 5(1):7-10. Epub 2010 Feb 16.
78. Zibert JR *et al.* Halting angiogenesis by non-viral somatic gene therapy alleviates psoriasis and murine psoriasiform skin lesions. *J Clin Invest* 2011 Jan 4;121(1):410-21.
79. Smyth LG *et al.* Carbonic anhydrase IX expression in prostate cancer. *Prostate Cancer and Prostatic Diseases* 2009 Dec;13(2):178-181.
80. Paatero I *et al.* Interaction with ErbB4 promotes hypoxia-inducible factor-1 $\alpha$  signal-

Target Protein	Product Name	Product No.	Validated Applications
Granulin	Anti-GRN	HPA008763 <sup>76</sup>	IHC,WB,ICC-IF
Granulin	Anti-GRN	HPA028747 <sup>76</sup>	IHC,ICC-IF
GSTP1	Anti-GSTP1	HPA019869 <sup>77</sup>	IHC,WB,ICC-IF
HIF-1 alpha/HIF1A	Anti-HIF1A	HPA001275 <sup>78-81</sup>	IHC,ICC-IF
HJURP	Anti-HJURP	HPA008436 <sup>82-85</sup>	IHC,WB,ICC-IF
HMGCL	Anti-HMGCL	HPA004727 <sup>2</sup>	IHC,WB
HMGCR	Anti-HMGCR	HPA008338 <sup>86-88</sup>	IHC
HMGCR	Anti-HMGCR	AMAb90619	IHC
HORMAD1/CT46	Anti-HORMAD1	HPA037850 <sup>89</sup>	IHC
HSD17B14	Anti-HSD17B14	HPA021467	IHC,WB
IFI30	Anti-IFI30	HPA026650 <sup>90</sup>	IHC,WB,ICC-IF
IL3RA	Anti-IL3RA	HPA003539 <sup>91</sup>	IHC,WB
KDM5B/CT31	Anti-KDM5B	HPA027179 <sup>92-95</sup>	IHC,WB
KLK3/PSA	Anti-KLK3	HPA000764 <sup>96-98</sup>	IHC
LSP1	Anti-LSP1	HPA019693 <sup>99</sup>	IHC,WB
LSR	Anti-LSR	HPA007220 <sup>100,101</sup>	IHC,WB,ICC-IF
MMP2	Anti-MMP2	HPA001939 <sup>45</sup>	IHC
MRPS7	Anti-MRPS7	HPA022522 <sup>8</sup>	IHC,WB,ICC-IF
MRPL40	Anti-MRPL40	HPA006181 <sup>8,102</sup>	IHC,WB,ICC-IF
MRPS15	Anti-MRPS15	HPA028134 <sup>8</sup>	IHC,WB
MRPS22	Anti-MRPS22	HPA006083 <sup>8</sup>	IHC,WB,ICC-IF
MSX2	Anti-MSX2	HPA005652 <sup>68,103,104</sup>	IHC,WB
MUC1/CA15-3	Anti-MUC1	HPA004179	IHC
MUC1/CA15-3	Anti-MUC1	HPA007235	IHC
MUC1/CA15-3	Anti-MUC1	HPA008855 <sup>105</sup>	IHC
MX1/IFI-78K	Anti-MX1	HPA030917 <sup>106</sup>	IHC,WB
NBN	Anti-NBN	HPA001429	IHC,WB
NFATC2	Anti-NFATC2	HPA008789 <sup>107,108</sup>	IHC,WB



## HMGCR

The Anti-HMGCR antibody (AMAb90619) shows moderate to strong cytoplasmic positivity in tumor cells in human breast cancer tissue samples using IHC. By WB, HMGCR can be detected in MCF-7 and HepG2 cell lines.

ing. *J Biol Chem* 2012 Mar 23;287(13):9659-71.

81. Zbytek B *et al.* Putative role of HIF transcriptional activity in melanocytes and melanoma biology. *Dermatoendocrinol* 2013 Apr 1; 5(2):239-251. Epub 2013/04/01.

82. Hu Z *et al.* The expression level of HJURP has an independent prognostic impact and predicts the sensitivity to radiotherapy in breast cancer. *Breast Cancer Res* 2010;12(2):R18

83. Shuaib M *et al.* HJURP binds CENP-A via a highly conserved N-terminal domain and mediates its deposition at centromeres. *Proc Natl Acad Sci U S A* 2010 Jan 26;107(4):1349-54

84. de Tayrac M *et al.* Prognostic Significance of EDN/RB, HJURP, p60/CAF-1 and PDL14, Four New Markers in High-Grade Gliomas. *PLoS One* 2013 Sep 11;8(9):e73332.

85. Huang W *et al.* A Non-Synonymous Single Nucleotide Polymorphism in the HJURP Gene Associated with Susceptibility to Hepatocellular Carcinoma among Chinese. *PLoS One* 2016 Feb; 11(2):e0148618. Epub 2016 Feb 10.

86. Bjarnadottir O *et al.* Targeting HMG-CoA reductase with statins in a window-of-opportunity breast cancer trial. *Breast Cancer Res Treat* 2013 Apr;138(2):499-508.

87. Bengtsson E *et al.* HMG-CoA reductase expression in primary colorectal cancer correlates with favourable clinicopathological characteristics and an improved clinical outcome. *Diagn Pathol* 2014 Apr 7; 9:78. Epub 2014 Apr 7.

88. Gustbée E *et al.* Tumor-specific expression of HMG-CoA reductase in a population-based cohort of breast cancer patients. *BMC Clin Pathol* 2015; 15:8. Epub 2015 May 20.

89. Watkins J *et al.* Genomic complexity profiling reveals that HORMAD1 overexpression contributes to homologous recombination deficiency in triple-negative breast cancers. *Cancer Discov* 2015 May; 5(5):488-505. Epub 2015 Mar 13.

90. Xiang YJ *et al.* Absence of Gamma-Interferon-Inducible Lysosomal Thiol Reductase (GILT) Is Associated with Poor Disease-Free Survival in Breast Cancer Patients. *PLoS One* 2014; 9(10):e109449. Epub 2014 Oct 21.

91. Mansfield AS *et al.* Metastasis to sentinel lymph nodes in breast cancer is associated with maturation arrest of dendritic cells and poor co-localization of dendritic cells and CD8+ T cells. *Virchows Arch* 2011 Oct; 459(4):391-8. Epub 2011 Sep 6.

92. Yamamoto S *et al.* JARID1B is a luminal lineage-driving oncogene in breast cancer. *Cancer Cell* 2014 Jun 16; 25(6):762-777.

93. Zou MR *et al.* Histone Demethylase Jumonji AT-rich Interactive Domain 1B (JARID1B) Controls Mammary Gland Development by Regulating Key Developmental and Lineage Specification Genes. *J Biol Chem* 2014 Jun 20; 289(25):17620-17633. Epub 2014 May 6.

94. Wang L *et al.* Overexpression of JARID1B is associated with poor prognosis and chemotherapy resistance in epithelial ovarian cancer. *Tumour Biol* 2015 Apr; 36(4):2465-2472. Epub 2015 Feb 8.

95. Hayami S *et al.* Overexpression of the JmJc histone demethylase KDM5B in human carcinogenesis: involvement in the proliferation of cancer cells through the E2F/RB pathway. *VMol Cancer* 2010 Mar 13; 9:59. Epub 2010 Mar 13.

96. Jaraj SJ *et al.* GAD1 is a biomarker for benign and malignant prostatic tissue. *Scand J Urol Nephrol* 2011 Feb;45(1):39-45.

97. Liu H *et al.* Single-cell clones of liver cancer stem cells have the potential of differentiating into different types of tumor cells. *Cell Death Dis* 2013 Oct; 4(10):e857-. Epub 2013/10/17.

98. Goto Y *et al.* MicroRNA expression signature of castration-resistant prostate cancer: the microRNA-221/222 cluster functions as a tumour suppressor and disease progression marker. *British Journal of Cancer* September 01, 2015.

99. Johansson J *et al.* TGF-β1-Induced Epithelial-Mesenchymal Transition Promotes Monocyte/Macrophage Properties in Breast Cancer Cells. *Front Oncol* 2015; 5:3. Epub 2015 Jan 26.

100. Sohet F *et al.* LSR/angulin-1 is a tricellular tight junction protein involved in blood-brain barrier formation. *J Cell Biol* 2015 Mar 16; 208(6):703-711.

101. Reaves DK *et al.* The Role of Lipolysis Stimulated Lipoprotein Receptor in Breast Cancer and Directing Breast Cancer Cell Behavior. *PLoS One* 2014; 9(3):e91747. Epub 2014 Mar 17.

102. Tappenden DM *et al.* The Aryl-Hydrocarbon Receptor Protein Interaction Network (AHR-PIN) as Identified by Tandem Affinity Purification (TAP) and Mass Spectrometry. *J Toxicol* 2013; 2013:279829. Epub 2013 Dec 5.

103. Wirrig EE *et al.* Differential expression of cartilage and bone-related proteins in pediatric and adult diseased aortic valves. *J Mol Cell Cardiol* 2011 Mar; 50(3):561-569. Epub 2010 Dec 14.

104. Wensman H *et al.* Extensive expression of craniofacial related homeobox genes in canine mammary sarcomas. *Breast Cancer Res Treat* 2009 Nov; 118(2):333-43. Epub 2008 Dec 2.

105. Lawson DA *et al.* Single-cell analysis reveals a stem-cell program in human metastatic breast cancer cells. *Nature* 2015 Oct 1; 526(7571):131-135. Epub 2015 Sep 23.

106. Johansson HJ *et al.* Proteomics profiling identify CAPS as a potential predictive marker of tamoxifen resistance in estrogen receptor positive breast cancer. *Clin Proteomics* 2015; 12(1):8. Epub 2015 Mar 21.

107. Scanlon CS *et al.* Galanin modulates the neural niche to favour perineural invasion

in head and neck cancer. *Nat Commun* 2015 Apr 28; 6:6885. Epub 2015 Apr 28.

108. Tran Quang C *et al.* The calcineurin/NFAT pathway is activated in diagnostic breast cancer cases and is essential to survival and metastasis of mammary cancer cells. *Cell Death Dis* 2015 Feb 26; 6(2):e1658-. Epub 2015 Feb 26.

109. Yoo NJ *et al.* Expression of NRF2, a cytoprotective protein, in gastric carcinomas. *APMIS* 2010 Aug; 118(8):613-4.

110. Suchocki P *et al.* Selenitetrigerides affect CYP1A1 and QR activity by involvement of reactive oxygen species and Nrf2 transcription factor. *Pharmacol Rep* 2010 Mar-Apr; 62(2):352-61.

111. Venkova K *et al.* Semaphorin 3A Signaling Through Neuropilin-1 Is an Early Trigger for Distal Axonopathy in the SOD1G93A Mouse Model of Amyotrophic Lateral Sclerosis. *J Neuropathol Exp Neurol* 2014 Jul; 73(7):702-713. Epub 2014 Jun 19.

112. Kim JH *et al.* OGFOD1 is required for breast cancer cell proliferation and is associated with poor prognosis in breast cancer. *Oncotarget* 2015 Aug 14; 6(23):19528-19541. Epub 2015 Mar 29.

113. Loenarz C *et al.* Hydroxylation of the eukaryotic ribosomal decoding center affects translational accuracy. *Proc Natl Acad Sci U S A* 2014 Mar 18; 111(11):4019-4024. Epub 2014 Feb 18.

114. Wehner KA *et al.* OGFOD1, a novel modulator of eukaryotic translation initiation factor 2alpha phosphorylation and the cellular response to stress. *Mol Cell Biol* 2010 Apr; 30(8):2006-16. Epub 2010 Feb 12.

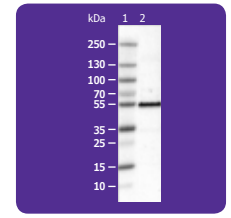
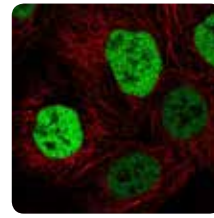
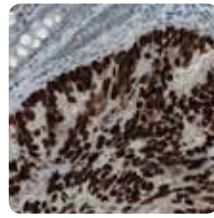
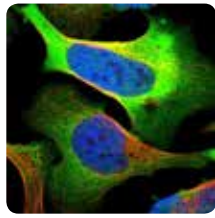
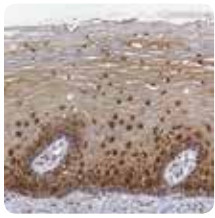
115. Guo L *et al.* Stat3-coordinated Lin-28-let-7-HMGA2 and miR-200-ZEB1 circuits initiate and maintain oncostatin M-driven epithelial-mesenchymal transition. *Oncogene* 2013 Nov 7;32(45):5272-82.

116. Hedström E *et al.* Downregulation of the cancer susceptibility protein WRAP53β in epithelial ovarian cancer leads to defective DNA repair and poor clinical outcome. *Cell Death Dis* 2015 Oct 1; 6(10):e1892-. Epub 2015 Oct 1.

117. O'Leary PC *et al.* Peroxiredoxin-1 protects estrogen receptor α from oxidative stress-induced suppression and is a protein biomarker of favorable prognosis in breast

Target Protein	Product Name	Product No.	Validated Applications
NFE2L2/HEBP1	Anti-NFE2L2	HPA002990 <sup>8,109,110</sup>	IHC
NRF1	Anti-NRF1	HPA029329 <sup>8</sup>	IHC,WB,ICC-IF
NRP1	Anti-NRP1	HPA030278 <sup>111</sup>	IHC
OGFOD1	Anti-OGFOD1	HPA003215 <sup>25,112-114</sup>	IHC,WB,ICC-IF
Oncostatin M	Anti-OSM	HPA029814 <sup>115</sup>	IHC,WB
P53	Anti-P53	AMAb90956 <sup>116</sup>	IHC,WB,ICC-IF
Peroxiredoxin-1	Anti-PRDX1	HPA007730 <sup>117-119</sup>	IHC,WB,ICC-IF
PHGDH	Anti-PHGDH	HPA021241 <sup>120-123</sup>	IHC,WB*,ICC-IF
PHGDH	Anti-PHGDH	AMAb90786	IHC,WB
PGD	Anti-PGD	HPA031314	IHC,WB*,ICC-IF
PIP/GCDFP	Anti-PIP	HPA009177	IHC,WB
Pirin	Anti-PIR	HPA000697 <sup>70</sup>	IHC,WB,ICC-IF
PKC alpha/PKCA	Anti-PKCA	HPA006563	IHC,WB*,ICC-IF
PKC alpha/PKCA	Anti-PKCA	HPA006564	IHC,WB*,ICC-IF
PLAT	Anti-PLAT	HPA003412	IHC,WB
POLRMT	Anti-POLRMT	HPA006366 <sup>8,124</sup>	IHC,ICC-IF
PPP4R1	Anti-PPP4R1	HPA041089 <sup>125,126</sup>	IHC,WB
PSMC3IP	Anti-PSMC3IP	HPA044439 <sup>127</sup>	IHC,WB
PSMC4/TBP-7	Anti-PSMC4	HPA002044 <sup>128</sup>	IHC,WB,ICC-IF
PSPH	Anti-PSPH	HPA020376 <sup>129,130</sup>	IHC,WB
PTMA	Anti-PTMA	HPA047183	IHC,ICC-IF
PTTG1	Anti-PTTG1	HPA008890	IHC
RAP80/UIMC1	Anti-UIMC1	HPA037503	IHC,WB,ICC-IF
RAP80/UIMC1	Anti-UIMC1	HPA037504	IHC,WB,ICC-IF
RBM3	Anti-RBM3	HPA003624 <sup>131-132,14</sup>	IHC,WB*,ICC-IF
RBM3	Anti-RBM3	AMAb90655 <sup>133-136</sup>	IHC,WB

\* WB both in human and rodent samples



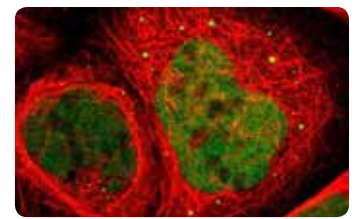
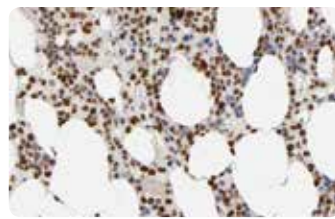
## PHGDH

Immunohistochemical staining of human cervix, uterine using Anti-PHGDH (HPA021241) antibody shows cytoplasmic and nuclear positivity in squamous epithelia. By Western Blot analysis, PHGDH is detected in the human cell lines RT-4 and U-251MG. ICC-IF in the human cell line U-2 OS shows positivity in plasma membrane & cytoplasm (in green).

- cancer. *Breast Cancer Res* 2014 Jul 10; 16(4):R79. Epub 2014 Jul 10.
118. Kamper P *et al.* Proteomic analysis identifies galectin-1 as a predictive biomarker for relapsed/refractory disease in classical Hodgkin lymphoma. *Blood* 2011 Jun 16; 117(24):6638-49. Epub 2011 Apr 19.
119. Dammeyer P and Arnér ES. Human Protein Atlas of redox systems - what can be learnt?. *Biochim Biophys Acta* 2011 Jan; 1810(1):111-38. Epub 2010 Jul 18.
120. Possemato R *et al.* Functional genomics reveal that the serine synthesis pathway is essential in breast cancer. *Nature* 2011 Aug 18;476(7360):346-50.
121. Maddocks OD *et al.* Serine starvation induces stress and p53-dependent metabolic remodelling in cancer cells. *Nature* 2013 Jan 24;493(7433):542-6.
122. Pacold ME *et al.* A PHGDH inhibitor reveals coordination of serine synthesis and one-carbon unit fate. *Nature Chemical Biology* 2013 April 25, 2016.
123. DeNicola GM *et al.* NRF2 regulates serine biosynthesis in non-small cell lung cancer. *Nat Genet* 2015/12/01; 47(12):1475-1481. Epub 2015 Oct 19.
124. Salem AF *et al.* Mitochondrial biogenesis in epithelial cancer cells promotes breast cancer tumor growth and confers autophagy resistance. *Cell Cycle* 2012 Nov 15; 11(22):4174-4180.
125. Wu G *et al.* PP4R1 accelerates cell growth and proliferation in HepG2 hepatocellular carcinoma. *Onco Targets Ther* 2015; 8:2067-2074. Epub 2015 Aug 7.
126. Qi Y *et al.* Lentivirus-Mediated Short-Hairpin RNA Targeting Protein Phosphatase 4 Regulatory Subunit 1 Inhibits Growth in Breast Cancer. *J Breast Cancer* 2015 Sep; 18(3):218-224. Epub 2015 Sep 24.
127. Capdevila-Busquets E *et al.* Breast Cancer Genes PSMC3IP and EPSTI1 Play a Role in Apoptosis Regulation. *PLoS One* 2015; 10(1):e0115352. Epub 2015 Jan 15.
128. Chen Y *et al.* Differential expression of novel tyrosine kinase substrates during breast cancer development. *Mol Cell Proteomics* 2007 Dec; 6(12):2072-87. Epub 2007 Sep 12.
129. Krall AS *et al.* Asparagine promotes cancer cell proliferation through use as an amino acid exchange factor. *Nat Commun* 2016 Apr 29; 7:11457. Epub 2016 Apr 29.
130. Possemato R *et al.* Functional genomics reveal that the serine synthesis pathway is essential in breast cancer. *Nature* 2011 Aug 18; 476(7360):346-50. Epub 2011 Aug 18.
131. Jögi A *et al.* Nuclear expression of the RNA-binding protein RBM3 is associated with an improved clinical outcome in breast cancer. *Mod Pathol* 2009 Dec;22(12):1564-74.
132. Hjelm B *et al.* High nuclear RBM3 expression is associated with an improved prognosis in colorectal cancer. *Proteomics Clin Appl* 2011 Dec;5(11-12):624-35.
133. Ehlén A *et al.* Expression of the RNA-binding protein RBM3 is associated with a favourable prognosis and cisplatin sensitivity in epithelial ovarian cancer. *J Transl Med* 2010 Aug 20;8:78.
134. Nodin B *et al.* High MCM3 expression is an independent biomarker of poor prognosis and correlates with reduced RBM3 expression in a prospective cohort of malignant melanoma. *Diagn Pathol* 2012 Jul 17;7:82.
135. Florianova L *et al.* Evaluation of RNA-binding motif protein 3 expression in urothelial carcinoma of the bladder: an immunohistochemical study. *World J Surg Oncol* 2015 Nov 14; 13(11):317.
136. Olofsson SE *et al.* Low RBM3 Protein Expression Correlates with Clinical Stage, Prognostic Classification and Increased Risk of Treatment Failure in Testicular Non-Seminomatous Germ Cell Cancer. *PLoS One* 2015; 10(3):e0121300.
137. Vanharanta S *et al.* Loss of the multifunctional RNA-binding protein RBM47 as a source of selectable metastatic traits in breast cancer. *eLife* 2014 Jun 4; 3:e02734. Epub 2014 Jun 4.
138. Telikicherla D *et al.* Overexpression of ribosome binding protein 1 (RRBP1) in breast cancer. *Clin Proteomics* 9(1):7. Epub 2012 Jun 18.
139. Ferrari N *et al.* Expression of RUNX1 Correlates with Poor Patient Prognosis in Triple

## P53

Immunohistochemical staining of human colorectal cancer using Anti-P53 (AMAb90956) antibody shows strong nuclear immunoreactivity in tumor cells. By Western Blot analysis, P53 is detected in the human cell line U-251. ICC-IF in the human cell line U-251 shows cell cycle dependent nuclear staining in green.



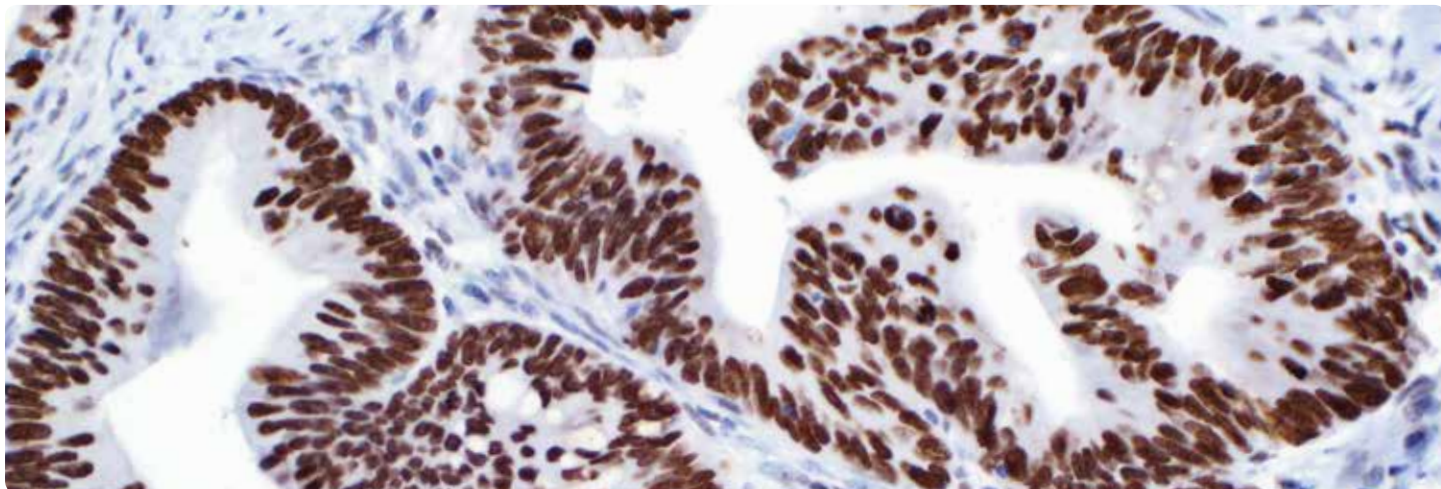
## RUNX1

IHC staining of human bone marrow using Anti-RUNX1 (HPA004176) antibody shows strong nuclear positivity in bone marrow poietic cells. ICC-IF in the human cell line A-431 shows positivity in nucleus and vesicles (in green).

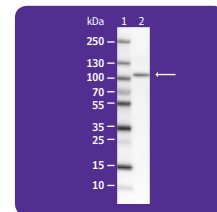
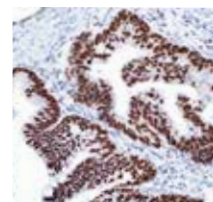
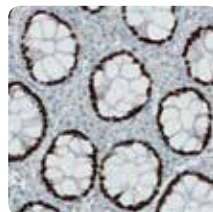
Target Protein	Product Name	Product No.	Validated Applications
RBM47	Anti-RBM47	HPA006347 <sup>137</sup>	IHC,WB,ICC-IF
RRBP1	Anti-RRBP1	HPA009026 <sup>138</sup>	IHC,WB,ICC-IF
RUNX1	Anti-RUNX1	HPA004176 <sup>139</sup>	IHC,WB,ICC-IF
RUNX2	Anti-RUNX2	HPA022040 <sup>140-142</sup>	IHC,WB,ICC-IF
SAGE1	Anti-SAGE1	HPA003208 <sup>143</sup>	IHC,ICC-IF
SATB2	Anti-SATB2	HPA001042 <sup>104,14,144,145</sup>	IHC,ICC-IF
SATB2	Anti-SATB2	AMAb90679	IHC,WB
Septin-11	Anti-SEPT11	HPA003459 <sup>146</sup>	IHC,WB
Septin-2	Anti-SEPT2	HPA018481 <sup>146,147</sup>	IHC,WB,ICC-IF
SIX1	Anti-SIX1	HPA001893 <sup>148-151</sup>	IHC,WB,ICC-IF
SIX1	Anti-SIX1	AMAb90544	IHC,WB
SNCG	Anti-SNCG	HPA014404	IHC,WB
STK11	Anti-STK11	HPA017254 <sup>152</sup>	IHC,WB,ICC-IF
SURVivin/BIRC5	Anti-BIRC5	HPA002830	IHC,WB

\* WB both in human and rodent samples

- Negative Breast Cancer. *PLoS One* 2014; 9(6):e100759. Epub 2014 Jun 26.
140. McDonald L *et al.* RUNX2 correlates with subtype-specific breast cancer in a human tissue microarray, and ectopic expression of Runx2 perturbs differentiation in the mouse mammary gland. *Dis Model Mech* 2014 May; 7(5):525-534. Epub 2014 Mar 13.
141. Ferrari N *et al.* Runx2 contributes to the regenerative potential of the mammary epithelium. *Sci Rep* 2015 Oct 22; 5:15658. Epub 2015 Oct 22.
142. Martínez-Abadías N *et al.* From shape to cells: mouse models reveal mechanisms altering palate development in Apert syndrome. *Dis Model Mech* 2013 May; 6(3):768-779. Epub 2013 Mar 8.

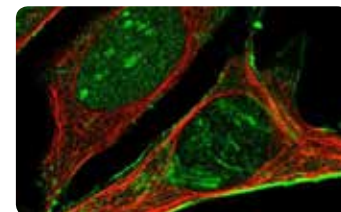


143. Maheswaran E *et al.* Lack of ADAM2, CALR3 and SAGE1 Cancer/Testis Antigen Expression in Lung and Breast Cancer. *PLoS One* 2015; 10(8):e0134967. Epub 2015 Aug 7.
144. Magnusson K *et al.* SATB2 in combination with cytokeratin 20 identifies over 95% of all colorectal carcinomas. *Am J Surg Pathol* 2011 Jul; 35(7):937-48.
145. Ek S *et al.* From gene expression analysis to tissue microarrays: a rational approach to identify therapeutic and diagnostic targets in lymphoid malignancies. *Mol Cell Proteomics* 2006 Jun; 5(6):1072-81. Epub 2006 Mar 8.
146. Froidevaux-Klipfel L *et al.* Modulation of septin and molecular motor recruitment in the microtubule environment of the Taxol-resistant human breast cancer cell line MDA-MB-231. *Proteomics* 2011 Oct; 11(19):3877-86. Epub 2011 Aug 18.
147. Volceanov L *et al.* Septins Arrange F-Actin-Containing Fibers on the Chlamydia trachomatis Inclusion and Are Required for Normal Release of the Inclusion by Extrusion. *mBio* 2014 Oct 7; 5(5):e01802-14. Epub 2014 Oct 7.
148. Iwanaga R *et al.* Expression of Six1 in luminal breast cancers predicts poor prognosis and promotes increases in tumor initiating cells by activation of extracellular signal-regulated kinase and transforming growth factor-beta signaling pathways. *Breast Cancer Res* 2012 Jul 5;14(4):R100.
149. Smith AL *et al.* The miR-106b-25 cluster targets Smad7, activates TGF- $\beta$  signaling, and induces EMT and tumor initiating cell characteristics downstream of Six1 in human breast cancer. *Oncogene* 2012 Jan 30;
150. Christina G *et al.* The Six1 oncoprotein downregulates p53 via concomitant regulation of RPL26 and microRNA-27a-3p. *Nature Communications* 2015 Dec 21;6:10077.
151. Ono H *et al.* SIX1 promotes epithelial-mesenchymal transition in colorectal cancer through ZEB1 activation. *Oncogene* 2012 Nov 22;31(47):4923-34.
152. Co NN *et al.* Loss of LKB1 in High Grade Endometrial Carcinoma: LKB1 is a Novel Transcriptional Target of p53. *Cancer* 2014 Nov 15; 120(22):3457-3468. Epub 2014 Jul 16.
153. Sembo S *et al.* Nuclear T-STAR Protein Expression Correlates with HER2 Status, Hormone Receptor Negativity and Prolonged Recurrence Free Survival in Primary Breast Cancer and Decreased Cancer Cell Growth In Vitro. *PLoS One* 2013; 8(7):e70596. Epub 2013 Jul 29.
154. Xu Y *et al.* The co-expression of MMP-9 and Tenascin-C is significantly associated with the progression and prognosis of pancreatic cancer. *Diagn Pathol*, 2015/12/10; 10:211. Epub 2015 Dec 10.
155. Ghosh Z *et al.* Dissecting the Oncogenic Potential of Human Embryonic and Induced Pluripotent Stem Cell Derivatives. *Cancer Res* 2011 Jul 15; 71(14):5030-5039. Epub 2011 Jun 6.
156. Bohonowych J *et al.* Extracellular Hsp90 mediates an NF- $\kappa$ B dependent inflammatory stromal program: Implications for the prostate tumor microenvironment. *Prostate*, 2014 Apr; 74(4):395-407. Epub 2013 Dec 16.
157. Edlund K *et al.* CD99 is a novel prognostic stromal marker in non-small cell lung cancer. *Int J Cancer* 2012 Nov 15;131(10):2264-73.



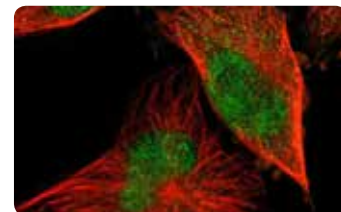
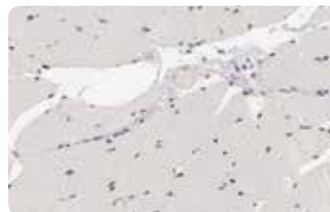
**SATB2**

The Anti-SATB2 antibody (AMAb90679) shows strong nuclear reactivity in glandular cells in human rectum tissue using IHC. By WB, SATB2 can be detected in the human cell line HEL.



**SEPT2**

The Anti-SEPT2 antibody (HPA018481) shows distinct cytoplasmic positivity in astrocytes and endothelial cells in cerebral cortex, using IHC. By ICC-IF in cell line U-2 OS, positivity in nucleus, nucleoli & actin filaments is shown.



**SIX1**

IHC staining using the Anti-SIX1 antibody (HPA001893) in human skeletal muscle tissue shows nuclear positivity in myocytes. ICC-IF staining in U-251 cell line shows positivity in nucleus in green.

158. Davidson B et al. Gene expression signatures differentiate ovarian/peritoneal serous carcinoma from breast carcinoma in effusions. *J Cell Mol Med* 2011 Mar;15(3):535-44.

159. Pontén F et al. The Human Protein Atlas—a tool for pathology. *J Pathol* 2008 Dec;216(4):387-93.

160. Wu CC et al. Candidate serological biomarkers for cancer identified from the secretomes of 23 cancer cell lines and the human protein atlas. *Mol Cell Proteomics* 2010 Jun;9(6):1100-17.

161. Lindén M et al. Tumour expression of bladder cancer-associated urinary proteins. *BJU Int* 2013 Aug; 112(3):407-15. Epub 2013 Mar 7.

162. Andersson S et al. Antibodies Biotinylated Using a Synthetic Z-domain from Protein A Provide Stringent In Situ Protein Detection. *J Histochem Cytochem* 2013 Nov; 61(11):773-784.

163. Dziegiel P et al. Ceramide galactosyltransferase (UGT8) is a molecular marker of breast cancer malignancy and lung metastases. *Br J Cancer* 2010 Aug 10;103(4):524-31.

164. Boerman GH et al. Role of NKG2D, DNAM-1 and natural cytotoxicity receptors in cytotoxicity toward rhabdomyosarcoma cell lines mediated by resting and IL-15-activated human natural killer cells. *Cancer Immunol Immunother* 2015 May; 64(5):573-583. Epub 2015 Feb 18.

165. Cho H et al. MICA/B and ULBP1 NKG2D ligands are independent predictors of good prognosis in cervical cancer. *BMC Cancer* 2014 Dec 15; 14:957. Epub 2014 Dec 15.

166. de Kruijff EM et al. NKG2D ligand tumor expression and association with clinical outcome in early breast cancer patients: an observational study. *BMC Cancer* 2012 Jan 18.

167. Salzano M et al. Vaccinia-related kinase 1 (VRK1) confers resistance to DNA-damaging agents in human breast cancer by affecting DNA damage response. *Oncotarget* 2014 Apr 15; 5(7):1770-1778. Epub 2014 Jan 17.

168. Kim IJ et al. Rewiring of human lung cell lineage and mitotic networks in lung adenocarcinomas. *Nat Commun* 2013; 4:1701.

169. Molitor TP et al. Molecular genetic analysis of VRK1 in mammary epithelial cells: depletion slows proliferation in vitro and tumor growth and metastasis in vivo. *Oncogenesis* 2013 Jun 3; 2(6):e48-. Epub 2013 Jun 3.

170. Cantarero L et al. VRK1 regulates Cajal body dynamics and protects coilin from proteasomal degradation in cell cycle. *Sci Rep* 2015 Jun 12; 5:10543. Epub 2015 Jun 12.

171. García E et al. WIP and WICH/WIRE co-ordinately control invadopodium formation and maturation in human breast cancer cell invasion. *Sci Rep* 2016 Mar 24; 6:23590. Epub 2016 Mar 24.

172. Wu SK et al. Active contractility at E-cadherin junctions and its implications for cell extrusion in cancer. *Cell Cycle* 2015; 14(3):315-322. Epub 2015 Feb 1.

173. Wu SK et al. Cortical F-actin stabilization generates apical-lateral patterns of junctional contractility that integrate cells into epithelia. *Nat Cell Biol* 2014 Feb; 16(2):167-78. Epub 2014 Jan 12.

174. Kovacs EM et al. N-WASP regulates the epithelial junctional actin cytoskeleton through a non-canonical post-nucleation pathway. *Nat Cell Biol* 2011 Jul 24; 13(8):934-43. Epub 2011 Jul 24.

175. Felzen V et al. Estrogen receptor  $\alpha$  regulates non-canonical autophagy that provides stress resistance to neuroblastoma and breast cancer cells and involves BAG3 function. *Cell Death Dis* 2015 Jul 9; 6(7):e1812-. Epub 2015 Jul 9.

176. Werner S et al. Dual Roles of the Transcription Factor Grainyhead-like 2 (GRHL2) in Breast Cancer. *J Biol Chem* 2013 Aug 9; 288(32):22993-23008. Epub 2013 Jun 29.

177. Jakobsen KR et al. Direct RNA sequencing mediated identification of mRNA localized in protrusions of human MDA-MB-231 metastatic breast cancer cells. *J Mol Signal* 2013 Sep 1; 8:9. Epub 2013 Sep 1.

178. Lehmann W et al. ZEB1 turns into a transcriptional activator by interacting with YAP1 in aggressive cancer types. *Nat Commun* 2016 Feb; 7:10498. Epub 2016 Feb 15.

179. De Sousa E Melo F et al. Poor-prognosis colon cancer is defined by a molecularly distinct subtype and develops from serrated precursor lesions. *Nat Med* 2013 May; 19(5):614-8. Epub 2013 Apr 14.

180. Müller S et al. Next-generation sequencing reveals novel differentially regulated mRNAs, lncRNAs, miRNAs, sdrRNAs and a piRNA in pancreatic cancer. *Mol Cancer* 2015 Apr 25; 14:94. Epub 2015 Apr 25.

181. Varma S et al. Grainyhead-like 2 (GRHL2) distribution reveals novel pathophysiological differences between human idiopathic pulmonary fibrosis and mouse models of pulmonary fibrosis. *Am J Physiol Lung Cell Mol Physiol* 2014 Mar 1; 306(5):L405-L419. Epub 2013 Dec 27.

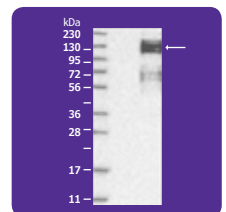
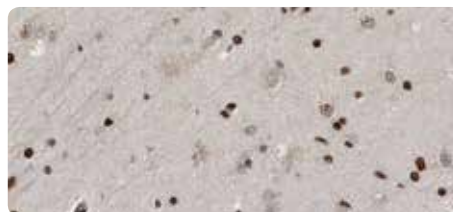
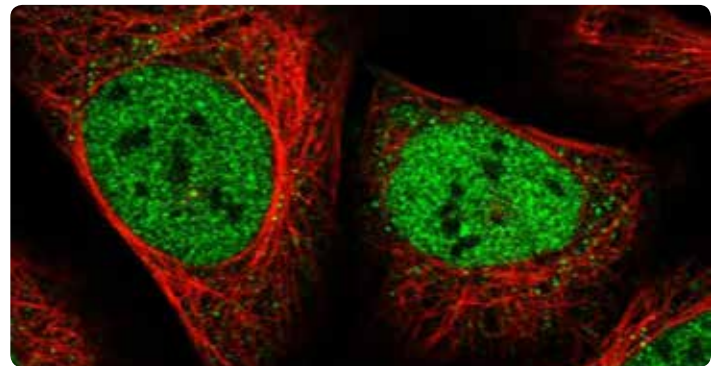
182. Denecker G et al. Identification of a ZEB2-MITF-ZEB1 transcriptional network that controls melanogenesis and melanoma progression. *Cell Death Differ* 2014 Aug; 21(8):1250-1261. Epub 2014 Apr 25.

183. Fang Y et al. Protein Expression of ZEB2 in Renal Cell Carcinoma and Its Prognostic Significance in Patient Survival. *PLoS One* 2013; 8(5):e62558. Epub 2013 May 2.

184. Cai MY et al. Overexpression of ZEB2 in Peritumoral Liver Tissue Correlates with Favorable Survival after Curative Resection of Hepatocellular Carcinoma. *PLoS One* 2012; 7(2):e32838. Epub 2012 Feb 29.

185. Holland DG et al. ZNF703 is a common Luminal B breast cancer oncogene that differentially regulates luminal and basal progenitors in human mammary epithelium. *EMBO Mol Med* 2011 Mar; 3(3):167-80. Epub 2011 Feb 18.

Target Protein	Product Name	Product No.	Validated Applications
Tenascin C/TNC	Anti-TNC	HPA004823 <sup>154-157</sup>	IHC,WB
TFAM/TCF-6	Anti-TFAM	HPA040648 <sup>8</sup>	IHC,WB,ICC-IF
TFF1	Anti-TFF1	HPA003425 <sup>158-160</sup>	IHC,WB
THBD	Anti-THBD	HPA002982	IHC,WB
THEM2/ACOT13	Anti-ACOT13	HPA019881	IHC,WB*,ICC-IF
TIMM9	Anti-TIMM9	HPA002932 <sup>8</sup>	IHC,WB,ICC-IF
TOMM70	Anti-TOM-M70A	HPA014589 <sup>8</sup>	IHC,WB,ICC-IF
TOP2A	Anti-TOP2A	HPA006458 <sup>161,162</sup>	IHC,WB,ICC-IF
TOP2A	Anti-TOP2A	HPA026773	IHC,ICC-IF
UGT8	Anti-UGT8	HPA014405 <sup>163</sup>	IHC,ICC-IF
ULBP1	Anti-ULBP1	HPA007547 <sup>164-166</sup>	IHC
VRK1	Anti-VRK1	HPA000660 <sup>167-170</sup>	IHC,WB,ICC-IF
WIPF2	Anti-WIPF2	HPA024467 <sup>171-174</sup>	IHC,WB
WIPI1	Anti-WIPI1	HPA007493 <sup>175</sup>	IHC,WB
ZEB1	Anti-ZEB1	HPA027524 <sup>176-179</sup>	IHC,WB,ICC-IF
ZEB1	Anti-ZEB1	AMAb90510 <sup>180,181</sup>	IHC,WB,ICC-IF
ZEB2	Anti-ZEB2	HPA003456 <sup>104,182-184</sup>	IHC,WB
ZNF703	Anti-ZNF703	HPA023930 <sup>185</sup>	IHC
ZNF703	Anti-ZNF703	AMAb90510	IHC,WB



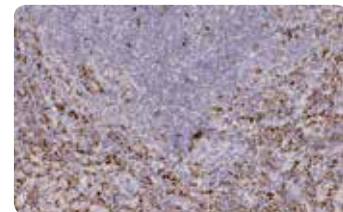
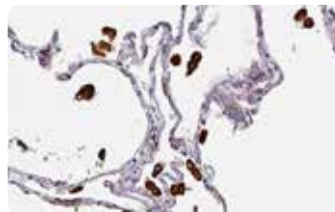
## ZEB1

Immunohistochemical staining of human cerebral cortex using Anti-ZEB1 (HPA027524) antibody shows strong nuclear positivity in glial cells. By Western Blot analysis, ZEB1 is detected in the human cell line U-251. ICC-IF in the human cell line U-2 OS shows positivity in nucleus, but excluded from the nucleoli (in green).

## Antibodies Against Gene Products in MammaPrint, Oncotype, EndoPredict and uPA Tests

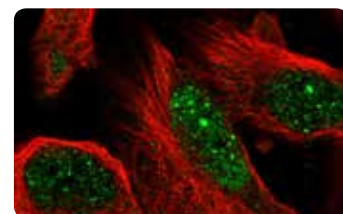
This section presents antibodies in the Prestige Antibody product catalog against gene products included in the diagnostic MammaPrint, EndoPredict, Oncotype and uPA tests. MammaPrint is a gene expression profile test based on the Amsterdam 70-gene breast cancer gene signature marketed by Agendia. It is a test to assess the risk that a breast tumor will metastasize to other parts of the body. MammaPrint aims at stratifying patients into “Low Risk” and “High Risk”. Oncotype DX (developed by Genomic Health) is the most frequently used gene expression profile in clinical practice in the United States analyzing a panel of 21 genes within a tumor to determine a Recurrence Score.

Target Protein	Product Name	Product No.	Validated Applications
AURKA/STK15	Anti-AURKA	HPA002636	IHC,WB
AZGP1	Anti-AZGP1	HPA012582	IHC,WB
BAG1	Anti-BAG1	HPA018121	IHC
BIRC5/Survivin	Anti-BIRC5	HPA002830	IHC,WB
CD68/Macrosialin	Anti-CD68	HPA048982 <sup>1</sup>	IHC
CD68/Macrosialin	Anti-CD68	AMAb90874	IHC,WB
CDCA7	Anti-CDCA7	HPA005565 <sup>2,3</sup>	IHC,WB,ICC-IF
CMC2/C16orf61	Anti-CMC2	HPA006871	IHC
DHCR7	Anti-DHCR7	HPA044280	IHC
DHX58/LGP2	Anti-DHX58	HPA018670	IHC,WB
DHX58/LGP2	Anti-DHX58	HPA019570	IHC
DIAPH3	Anti-DIAPH3	HPA032152	IHC,WB*
DTL	Anti-DTL	HPA028016 <sup>4</sup>	IHC,WB,ICC-IF
ECI2/PECI	Anti-ECI2	HPA022130	IHC,WB,ICC-IF
ECI2/PECI	Anti-ECI2	HPA031626	IHC,WB,ICC-IF
EGLN1/PHD2	Anti-EGLN1	HPA022129 <sup>5</sup>	IHC,ICC-IF
Estrogen receptor	Anti-ESR1	AMAb90867	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000449 <sup>6</sup>	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000450 <sup>6</sup>	IHC,WB
Exostosin-1	Anti-EXT1	HPA044394 <sup>7</sup>	IHC,WB
GNAZ	Anti-GNAZ	HPA003011	IHC,WB
GPR126/VIGR	Anti-GPR126	HPA017346	IHC
GPR180	Anti-GPR180	HPA047250	IHC,ICC-IF
GSTM3	Anti-GSTM3	HPA035190	IHC,WB
GSTM5/GSTM1	Anti-GSTM5	HPA048652	IHC,WB
HER2/ERBB2	Anti-HER2	AMAb90627	IHC,WB
HER2/ERBB2	Anti-HER2	AMAb90628	IHC,WB



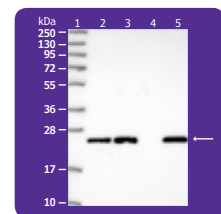
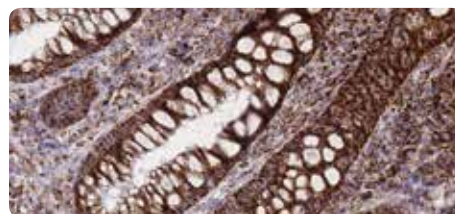
### CD68/Macrosialin

IHC staining of human lung tissue using the Anti-CD68 antibody (HPA048982) shows strong cytoplasmic positivity in macrophages and in hematopoietic tissues, such as spleen.



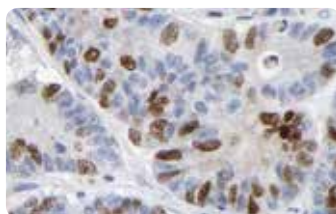
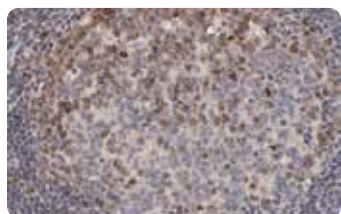
### DTL

IHC staining of human bone marrow using the Anti-DTL antibody (HPA028016) shows strong nuclear positivity in bone marrow poietic cells. By ICC-IF, staining of nucleus in U-251 MG cells is detected.



### GSTM5

The Anti-GSTM5 antibody (HPA048652) shows cytoplasmic positivity in glandular cells in human rectum by IHC and in WB, the antibody detects a band of predicted size in cell lysates of RT-4, U-251 MG, as well as in liver tissue lysate.

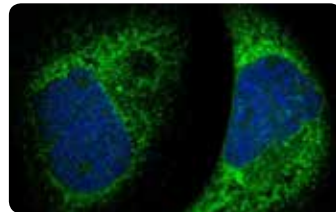
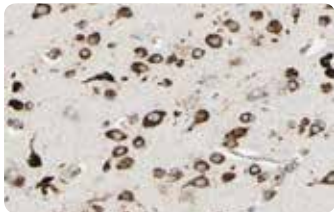


### BIRC5/Survivin

The Anti- BIRC5 antibody (HPA002830) shows nuclear positivity in germinal center cells in human tonsil tissue and in tumor cells in colorectal cancer using IHC.

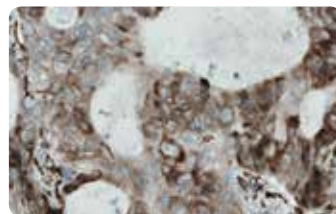
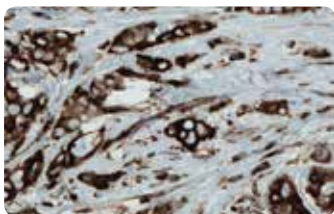


- Louveau A et al. Structural and functional features of central nervous system lymphatic vessels. *Nature* June 01, 2015.
- Gill RM et al. The MYC-Associated Protein CDCA7 Is Phosphorylated by AKT To Regulate MYC-Dependent Apoptosis and Transformation. *Mol Cell Biol* 2013 Feb; 33(3):498-513.
- Shubbar E et al. Elevated cyclin B2 expression in invasive breast carcinoma is associated with unfavorable clinical outcome. *BMC Cancer* 131. Epub 2013/01/02.
- Karaayvaz M et al. Prognostic significance of miR-215 in colon cancer. *Clin Colorectal Cancer* 2011 Dec;10(4):340-7.
- Bozóky B et al. Novel signatures of cancer-associated fibroblasts. *Int J Cancer* 2013 Jul 15; 133(2):286-93. Epub 2013 Feb 12.
- Algenäs C et al. Antibody performance in western blot applications is context-dependent. *Biotechnol J* 2014 Mar; 9(3):435-45. Epub 2014 Jan 29.
- Coulson-Thomas VJ et al. Heparan Sulfate Regulates Hair Follicle and Sebaceous Gland Morphogenesis and Homeostasis. *J Biol Chem* 2014 Sep 5; 289(36):25211-25226. Epub 2014 Jul 22.
- Huvila J et al. Progesterone receptor negativity is an independent risk factor for relapse in patients with early stage endometrioid endometrial adenocarcinoma. *Gynecol Oncol* 2013 Sep; 130(3):463-9. Epub 2013 Jun 15.
- Newie I et al. The HER2-Encoded miR-4728-3p Regulates ESR1 through a Non-Canonical Internal Seed Interaction. *PLoS One* 2014; 9(5):e97200. Epub 2014 May 14.
- Rognum IJ et al. Interleukin-6 and the serotonergic system of the medulla oblongata in the sudden infant death syndrome. *Acta Neuropathol* 2009 Oct;118(4):519-3.
- Pohler E et al. Haploinsufficiency for AAGAB causes clinically heterogeneous forms of punctate palmoplantar keratoderma. *Nat Genet* 2012 Oct 14;44(11):1272-6.
- Li S et al. Endothelial VEGF Sculpts Cortical Cytoarchitecture. *J Neurosci* 2013 Sep 11; 33(37):14809-14815.
- Roca H et al. IL-4 induces proliferation in prostate cancer PC3 cells under nutrient-depletion stress through the activation of the JNK-pathway and survivin upregulation. *J Cell Biochem* 2012 May; 113(5):1569-1580.



### LYRIC/MTDH

IHC staining using the Anti-MTDH antibody (HPA010932) shows strong cytoplasmic positivity in neuronal cells in human cerebral cortex tissue. In ICC-IF in A-431 cell line, the antibody stains endoplasmic reticulum.



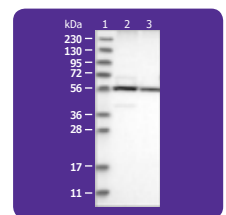
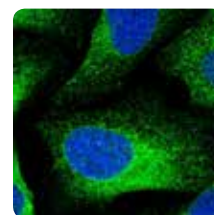
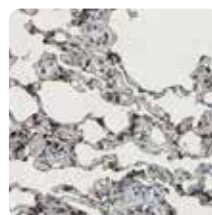
IHC staining using the monoclonal Anti-MTDH antibody (AMAb90762) shows strong cytoplasmic reactivity in tumor cells from breast and colorectal cancer samples.

- Friedman JS et al. Loss of lysophosphatidylcholine acyltransferase 1 leads to photoreceptor degeneration in rd11 mice. *Proc Natl Acad Sci U S A* 2010 Aug 31;107(35):15523-8.
- Dai X et al. AAV-Mediated Lysophosphatidylcholine Acyltransferase 1 (Lpcat1) Gene Replacement Therapy Rescues Retinal Degeneration in rd11 Mice. *Invest Ophthalmol Vis Sci* 2014 Mar 20; 55(3):1724-1734. Epub 2014 Mar 20.
- Nohata N et al. Tumor suppressive microRNA-375 regulates oncogene AEG-1/MTDH in head and neck squamous cell carcinoma (HNSCC). *J Hum Genet* 2011 Aug;56(8):595-601.

Target Protein	Product Name	Product No.	Validated Applications
HER2/ERBB2	Anti-ERBB2	HPA001383 <sup>8,9</sup>	IHC,WB,ICC-IF
HRASLS	Anti-HRASLS	HPA051179	IHC,ICC-IF
IL6ST/GP130	Anti-IL6ST	HPA010558 <sup>10</sup>	IHC
JHDM1D/KDM7A	Anti-JHDM1D	HPA012114	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	HPA000451 <sup>11,12</sup>	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	HPA001164 <sup>13</sup>	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	AMAb90870	IHC
LIN9	Anti-LIN9	HPA030241	IHC,ICC-IF
LPCAT1/AYTL2	Anti-LPCAT1	HPA012501	IHC,WB
LPCAT1/AYTL2	Anti-LPCAT1	HPA022268 <sup>14,15</sup>	IHC,WB
LYRIC/MTDH	Anti-MTDH	HPA015104 <sup>16,17</sup>	IHC,WB,ICC-IF
LYRIC/MTDH	Anti-MTDH	HPA010932 <sup>18</sup>	IHC,WB*,ICC-IF
LYRIC/MTDH	Anti-MTDH	AMAb90762	IHC,WB
LYRIC/MTDH	Anti-MTDH	AMAb90763	IHC,WB
Matrix Gla protein	Anti-MGP	HPA013949 <sup>19</sup>	IHC
MCM6	Anti-MCM6	HPA004818	IHC,WB*,ICC-IF
MELK/PK38	Anti-MELK	HPA017214	IHC
MMP9	Anti-MMP9	HPA001238 <sup>20,21</sup>	IHC,WB,ICC-IF
MMP9	Anti-MMP9	AMAb90804	IHC,WB
MMP9	Anti-MMP9	AMAb90805	IHC,WB
MMP9	Anti-MMP9	AMAb90806	IHC
MS4A7	Anti-MS4A7	HPA017418	IHC,WB

\* WB both in human and rodent samples

- Giopanou I et al. Metadherin, p50, and p65 Expression in Epithelial Ovarian Neoplasms: An Immunohistochemical Study. *Biomed Res Int* 2014; 2014:178410. Epub 2014 May 22.
- Liu B et al. Astrocyte elevated gene-1 regulates osteosarcoma cell invasion and chemoresistance via endothelin-1/endothelin A receptor signaling. *Oncol Lett* 2013 Feb;5(2):505-510.
- Lorenzen JM et al. Fetuin, matrix-Gla protein and osteopontin in calcification of renal allografts. *PLoS One* 2012;7(12):e52039.
- Bass JA et al. Investigation of potential early Histologic markers of pediatric inflammatory bowel disease. *BMC Gastroenterol* 2015 Oct 13; 15:129. Epub 2015 Oct 13.
- Song C et al. Histone Deacetylase (HDAC) 10 Suppresses Cervical Cancer Metastasis through Inhibition of Matrix Metalloproteinase (MMP) 2 and 9 Expression. *J Biol Chem* 2013 Sep 27; 288(39):28021-28033. Epub 2013 Jul 29.



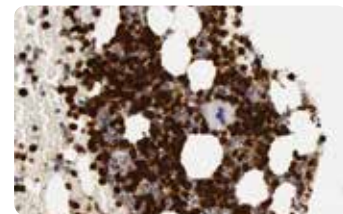
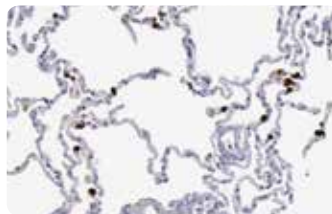
### LPCAT1/AYTL2

Immunohistochemical staining of human lung using Anti-LPCAT1 (HPA022268) antibody shows strong cytoplasmic positivity in pneumocytes. By Western Blot analysis, LPCAT1 is detected in the human cell lines RT-4 and U-251. ICC-IF in the human cell line U-2 OS shows positivity in endoplasmic reticulum (in green).

Target Protein	Product Name	Product No.	Validated Applications
MYBL2	Anti-MYBL2	HPA030530	IHC,WB
Neuromedin-U	Anti-NMU	HPA025926	IHC,WB
NUSAP1	Anti-NUSAP1	HPA042904	IHC,ICC-IF
P5C dehydrogenase	Anti-ALDH4A1	HPA006401	IHC,WB
PITRM1/MP1	Anti-PITRM1	HPA006753	IHC,WB,ICC-IF
PITRM1/MP1	Anti-PITRM1	HPA006754	IHC,WB*
PLAU/UPA	Anti-PLAU	HPA008719	IHC,WB
PRC1	Anti-PRC1	HPA034521	IHC,WB,ICC-IF
Progesteron receptor	Anti-PGR	HPA004751 <sup>22</sup>	IHC
Progesteron receptor	Anti-PGR	HPA008428 <sup>23</sup>	IHC
Progesteron receptor	Anti-PGR	HPA017176	IHC
QSOX2/QSCN6L1	Anti-QSOX2	HPA012716	IHC,WB,ICC-IF
RBBP8	Anti-RBBP8	HPA039890	IHC
RECQL5	Anti-RECQL5	HPA029970	IHC,ICC-IF
RECQL5	Anti-RECQL5	HPA029971 <sup>24</sup>	IHC,WB,ICC-IF
RTN4RL1/NgR3	Anti-RTN4RL1	HPA044428	IHC
RUNDC1	Anti-RUNDC1	HPA023726	IHC,WB,ICC-IF
SCUBE2/CEGP1	Anti-SCUBE2	HPA006353	IHC,ICC-IF
SCUBE2/CEGP1	Anti-SCUBE2	HPA029871	IHC
SCOT/OXCT1	Anti-OXCT1	HPA012047 <sup>25</sup>	IHC,WB*,ICC-IF
SCOT/OXCT1	Anti-OXCT1	HPA061425	IHC,ICC-IF
SERPINE1/PAI1	Anti-SER-PINE1	HPA050039 <sup>26</sup>	IHC
SLC2A3/GLUT3	Anti-SLC2A3	HPA006539 <sup>27,28</sup>	IHC
Stanniocalcin-2	Anti-STC2	HPA045372	IHC, WB, IF
STK32B	Anti-STK32B	HPA015820	IHC
TGFB3	Anti-TGFB3	HPA027923	IHC,WB
TMEM74B/C20orf46	Anti-TMEM74B	HPA045213	IHC
TSPYL5	Anti-TSPYL5	HPA031347	IHC,ICC-IF
UCHL5	Anti-UCHL5	HPA005908	IHC
VEGFR-1	Anti-FLT1	AMAb90703	IHC
VEGFR-1	Anti-FLT1	AMAb90704	IHC,WB
WISP1	Anti-WISP1	HPA007121	IHC,ICC-IF

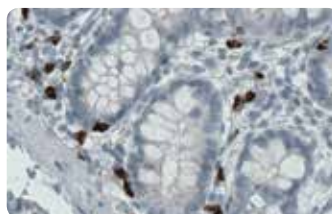
\* WB both in human and rodent samples

22. Pereira CB et al. Prognostic and Predictive Significance of MYC and KRAS Alterations in Breast Cancer from Women Treated with Neoadjuvant Chemotherapy. *PLoS One* 2013;8(3):e60576.
23. Huvila J et al. Progesterone receptor negativity is an independent risk factor for relapse in patients with early stage endometrioid endometrial adenocarcinoma. *Gynecol Oncol* 2013 Sep; 130(3):463-9. Epub 2013 Jun 15.
24. Lao VV et al. Altered RECQ Helicase Expression in Sporadic Primary Colorectal Cancers. *Transl Oncol.* 2013 Aug; 6(4):458-469. Epub 2013 Aug 1.
25. Chang HT et al. Ketolytic and glycolytic enzymatic expression profiles in malignant gliomas: implication for ketogenic diet therapy. *Nutr Metab (Lond)* 1047. Epub 2013/07/05.
26. Zhang G et al. Validation and clinicopathologic associations of a urine-based bladder cancer biomarker signature. *Diagn Pathol* 2014 Nov 12; 9:200. Epub 2014 Nov 12.
27. Munthe S et al. Glioma Cells in the Tumor Periphery Have a Stem Cell Phenotype. *PLOS ONE* May 12, 2016.
28. Wang W et al. AMPK modulates Hippo pathway activity to regulate energy homeostasis. *Nat Cell Biol* 2015 Apr; 17(4):490-499. Epub 2015 Mar 9.

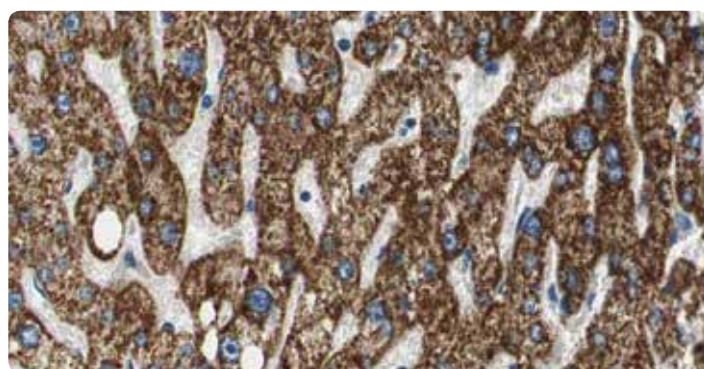
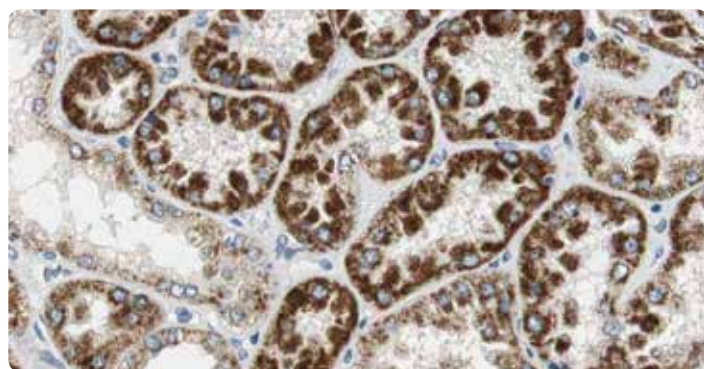


### MMP9

IHC staining of human lung tissue using the Anti-MMP9 antibody (HPA001238) shows strong nuclear positivity in macrophages and in bone marrow poietic cells in bone marrow tissue.

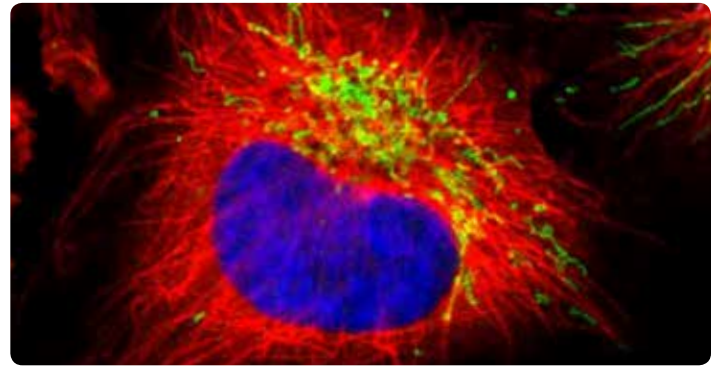
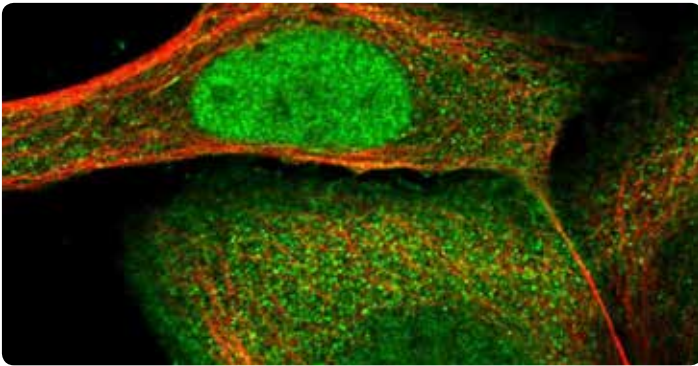
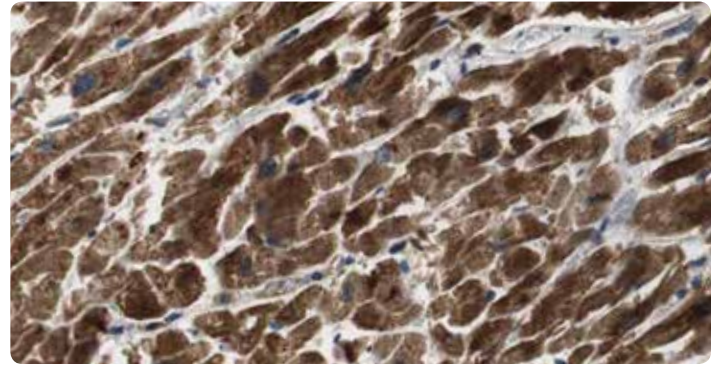
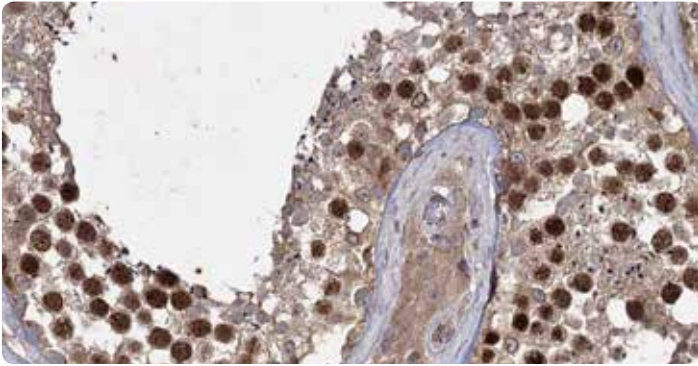


Monoclonal Anti-MMP9 antibodies show strong cytoplasmic positivity in a subset of lymphoid cells in duodenum (AMAb90805) and in human tonsil tissue (AMAb90804).



### P5C dehydrogenase/ALDH4A1

IHC staining using the Anti-ALDH4A1 antibody (HPA006401) shows strong cytoplasmic positivity with granular pattern in human kidney and liver tissues.

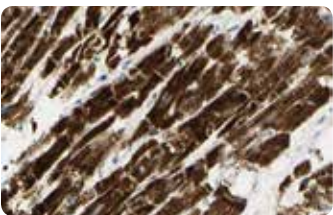
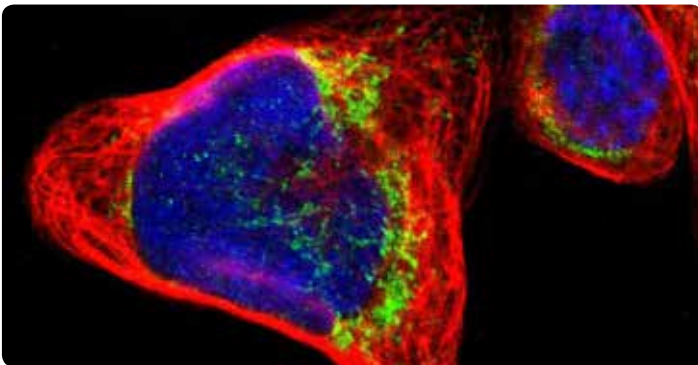


**PRC1**

IHC staining of human testis tissue using the Anti-PRC1 antibody (HPA034521) shows strong nuclear positivity in cells of seminiferous ducts. ICC-IF shows staining of nucleus, plasma membrane and microtubules in A-431 cells.

**PITRM1/MP1**

The Anti- PITRM1 antibody (HPA006753) shows strong cytoplasmic positivity in myocytes in human heart muscle using IHC. ICC-IF staining of human cell line U-251 MG shows positivity in mitochondria.



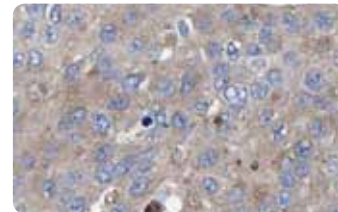
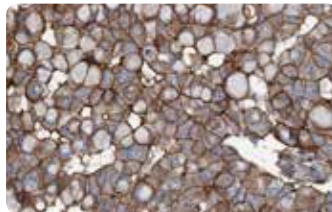
**SCOT/OXCT1**

IHC staining of human heart muscle and kidney by Anti-OXCT1 antibody (HPA028016) shows strong cytoplasmic positivity in myocytes and cells in tubules, respectively. ICC-IF shows staining of mitochondria in A431 cells.

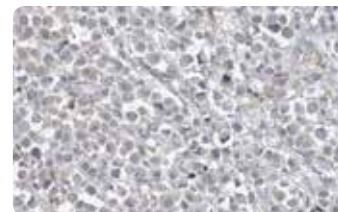
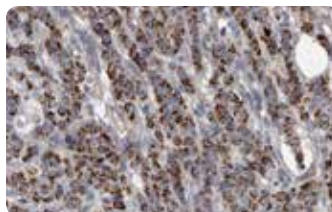
# Antibodies Identified in the Human Protein Atlas

Showing differential IHC staining patterns in breast cancer samples

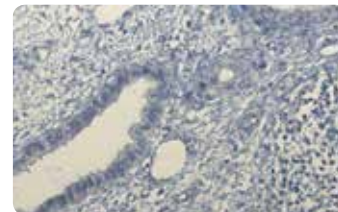
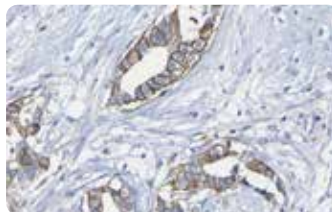
Target Protein	Product No.	Validated Applications
Anti-AAMDC	HPA037918	IHC,WB,ICC-IF
Anti-AAMDC	HPA037919	IHC,ICC-IF
Anti-ACSF2	HPA024693	IHC,WB,ICC-IF
Anti-ADAMTS13	HPA042014	IHC,WB
Anti-ADIRF	HPA026810	IHC,WB,ICC-IF
Anti-AGR3	HPA053942	IHC
Anti-AIF1L	HPA020522	IHC,WB
Anti-AJUBA	HPA006171 <sup>1</sup>	IHC,WB
Anti-ALDH1A3	HPA046271 <sup>2</sup>	IHC,WB,ICC-IF
Anti-ANKRD46	HPA013758	IHC,WB
Anti-ASB6	HPA004341	IHC,WB
Anti-ATF6	HPA005935	IHC
Anti-ATP6V1B2	HPA008147	IHC,WB,ICC-IF
Anti-AVPR2	HPA046678	IHC
Anti-BCL9	HPA020274	IHC,ICC-IF
Anti-C10orf54	HPA007968	IHC,WB,ICC-IF
Anti-C12orf76	HPA039713	IHC,WB
Anti-C17orf85	HPA008959 <sup>3</sup>	IHC,ICC-IF
Anti-C1ORF195	HPA045811	IHC
Anti-C2orf68	HPA051143	IHC,ICC-IF
Anti-CCDC170	HPA027185	IHC,WB
Anti-CDK6	HPA002637	IHC,WB,ICC-IF
Anti-CLDN3	HPA014361	IHC
Anti-CPNE2	HPA041132	IHC,WB
Anti-CRABP2	HPA004135 <sup>4</sup>	IHC,WB,ICC-IF
Anti-CTNND2	HPA015077	IHC
Anti-CXorf67	HPA006128	IHC,ICC-IF
Anti-CYP4X1	HPA017661	IHC,WB
Anti-DACH1	HPA012672 <sup>5-7</sup>	IHC,ICC-IF
Anti-DCHS1	HPA050246	IHC
Anti-DCLK1	HPA015655	IHC,WB
Anti-DOM3Z	HPA046708	IHC
Anti-ECD	HPA006465	IHC,WB,ICC-IF
Anti-EFHD1	HPA049331	IHC
Anti-EPHA6	HPA007397	IHC,WB,ICC-IF
Anti-FAM189A1	HPA009410	IHC,ICC-IF
Anti-FKBP7	HPA008707	IHC,WB,ICC-IF
Anti-GABRD	HPA044371	IHC
Anti-GAK	HPA027463	IHC,ICC-IF



IHC analysis using Anti-KLHL26 antibody (HPA023074) shows a varying membranous/cytoplasmic staining pattern in breast tumor samples from different patients.



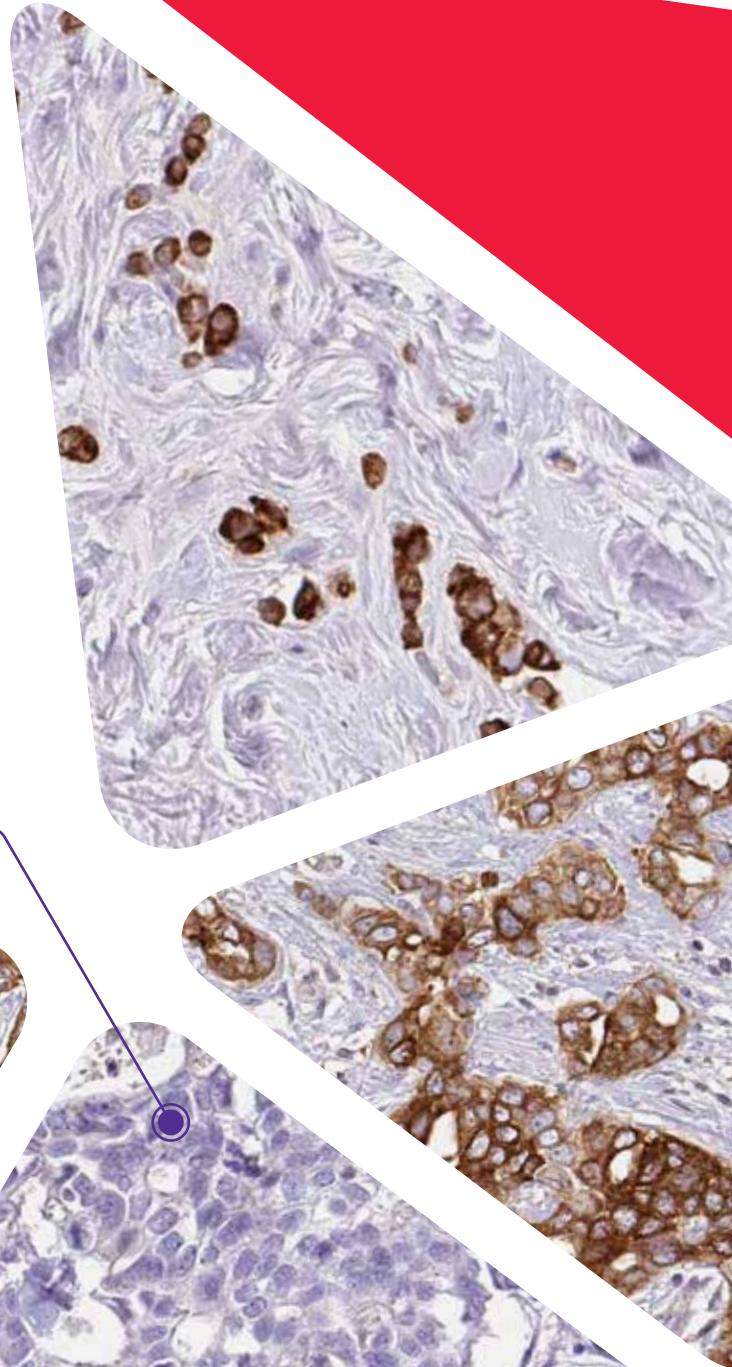
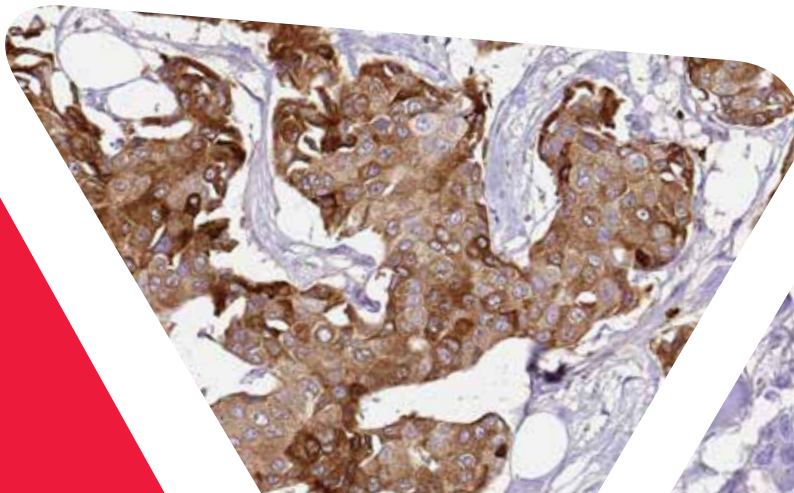
The Anti-ACSF2 (HPA024693) antibody shows granular cytoplasmic positivity in breast tumor cells from different patients varying from strong to negative.



The Anti-GCM1 (HPA011343) antibody shows membranous positivity in breast tumor cells while normal breast tissue is negative.

1. Tsuneki M et al. A hydrogel-endothelial cell implant mimics infantile hemangioma: modulation by survivin and the Hippo pathway. *Laboratory Investigation* 2015 95, 765–780.
2. Girardi RR et al. Stem and progenitor cell division kinetics during postnatal mouse mammary gland development. *Nat Commun* 2015 Oct 29; 6:8487. Epub 2015 Oct 29.
3. Gebhardt A et al. mRNA export through an additional cap-binding complex consisting of NCBP1 and NCBP3. *Nat Commun* 2015 Sep 18; 6:8192. Epub 2015 Sep 18.
4. Seidensaal K et al. Impaired aldehyde dehydrogenase 1 subfamily member 2A-dependent retinoic acid signaling is related with a mesenchymal-like phenotype and an unfavorable prognosis of head and neck squamous cell carcinoma. *Mol Cancer* 2015/12/03; 14:204. Epub 2015 Dec 3.
5. Zhou J et al. DACH1, a Zona Glomerulosa Selective Gene in the Human Adrenal, Activates Transforming Growth Factor- $\beta$  Signaling and Suppresses Aldosterone Secretion. *Hypertension* 2015 May; 65(5):1103-1110. Epub 2015 Apr 8.
6. Powe DG et al. DACH1: Its Role as a Classifier of Long Term Good Prognosis in Luminal Breast Cancer. *PLoS One* 2014; 9(1):e84428. Epub 2014 Jan 2.
7. Vonlanthen J et al. A comprehensive look at transcription factor gene expression changes in colorectal adenomas. *BMC Cancer* 2014 Jan 29; 14:46. Epub 2014 Jan 29.
8. Renaud SJ et al. OVO-like 1 regulates progenitor cell fate in human trophoblast development. *Proc Natl Acad Sci U S A* 2015/11/10; 112(45):E6175-E6184. Epub 2015 Oct 26.
9. Kim D et al. SHMT2 drives glioma cell survival in ischaemia but imposes a dependence on glycine clearance. *Nature* April 08, 2015.
10. Ngan E et al. A complex containing LPP and  $\alpha$ -Actinin mediates TGF  $\beta$ -induced migration and invasion of ErbB2-expressing breast cancer cells. *J Cell Sci* 2013 May 1; 126(09):1981-1991. Epub 2013/02/27.
11. Nagao M et al. Zbtb20 promotes astrocytogenesis during neocortical development. *Nat Commun* 1/01/01; 7:11102. Epub 2016 Mar 22.
12. Camilleri M et al. Neuropeptide S receptor induces neuropeptide expression and associates with intermediate phenotypes of functional gastrointestinal disorders. *Gastroenterology* 2010 Jan;138(1):98-107.e4.
13. Song Z et al. PRR11 Is a Prognostic Marker and Potential Oncogene in Patients with Gastric Cancer. *PLoS One* 2015; 10(8):e0128943. Epub 2015 Aug 7.
14. Chen Y et al. The prognostic potential and oncogenic effects of PRR11 expression in hilar cholangiocarcinoma. *Oncotarget* 2015 Aug 21; 6(24):20419-20433. Epub 2015 May 4.
15. Bozóky B et al. Novel signatures of cancer-associated fibroblasts. *Int J Cancer* 2013 Jan 15.
16. Peluffo H et al. CD300f immunoreceptor contributes to peripheral nerve regeneration by the modulation of macrophage inflammatory phenotype. *J Neuroinflammation* 2015 Aug 12; 12:145. Epub 2015 Aug 12.
17. Dinets A et al. Differential Protein Expression Profiles of Cyst Fluid from Papillary Thyroid Carcinoma and Benign Thyroid Lesions. *JPLoS One* 2015; 10(5):e0126472. Epub 2015 May 15.

The Anti-AGR3 (HPA053942) antibody shows strong cytoplasmic positivity in 11/12 breast cancer patients, while 1 patient is completely negative.



Target Protein	Product No.	Validated Applications	Target Protein	Product No.	Validated Applications
Anti-GCM1	HPA011343 <sup>8</sup>	IHC	Anti-S100A14	HPA027613	IHC,ICC-IF
Anti-GLDC	HPA002318 <sup>9</sup>	IHC,WB	Anti-S100A7	HPA006997	IHC
Anti-GLYATL1	HPA039501	IHC,WB	Anti-SGK196	HPA013321	IHC,WB,ICC-IF
Anti-GTF3A	HPA007990	IHC,ICC-IF	Anti-SH3BGRL	HPA051248	IHC,WB
Anti-HIPK2	HPA007611	IHC,ICC-IF	Anti-SHROOM1	HPA037690	IHC
Anti-HMGCS1	HPA036913	IHC,WB,ICC-IF	Anti-SIMC1	HPA037889	IHC,WB,ICC-IF
Anti-HMGCS2	HPA027423	IHC,WB	Anti-SLC16A7	HPA005911	IHC,WB
Anti-HMGCS2	HPA027442	IHC,WB,ICC-IF	Anti-SLC39A6	HPA042377	IHC,WB
Anti-IFITM3	HPA004337	IHC,WB	Anti-SPAG1	HPA023748	IHC,ICC-IF
Anti-IRX2	HPA054669	IHC,WB	Anti-SQLE	HPA018038 <sup>19</sup>	IHC,WB
Anti-ISYNA1	HPA007931	IHC,WB,ICC-IF	Anti-SRPRB	HPA011173	IHC,WB,ICC-IF
Anti-ISYNA1	HPA008232	IHC,WB	Anti-SSSCA1	HPA039789	IHC,WB,ICC-IF
Anti-ITGA3	HPA008572	IHC,WB	Anti-STAG3	HPA049106	IHC,WB
Anti-ITGBL1	HPA005676	IHC,WB	Anti-STARD6	HPA042583	IHC,IF
Anti-ITIH6	HPA000506	IHC	Anti-STX7	HPA001467 <sup>20</sup>	IHC,WB,ICC-IF
Anti-KLHL26	HPA023074	IHC,WB	Anti-TACC3	HPA005781 <sup>21</sup>	IHC,WB
Anti-KRT31	HPA049550	IHC	Anti-TAPBP	HPA007066	IHC
Anti-LASP1	HPA012072 <sup>10</sup>	IHC,WB,ICC-IF	Anti-TBC1D9	HPA000262	IHC,ICC-IF
Anti-LGR6	HPA008556	IHC	Anti-TGFBI	HPA017019	IHC,WB
Anti-LRRIQ4	HPA036706	IHC	Anti-TMEM222	HPA016579	IHC
Anti-MAGEB1	HPA002820	IHC	Anti-TMEM47	HPA046658	IHC
Anti-MANSC4	HPA039454	IHC	Anti-TMEM68	HPA018216	IHC,ICC-IF
Anti-MROH2B	HPA059457	IHC	Anti-TPX2	HPA005487	IHC,WB,ICC-IF
Anti-MRS2	HPA017642	IHC,WB	Anti-TTL12	HPA003054	IHC,WB,ICC-IF
Anti-MSTO1	HPA005914	IHC	Anti-UBE20	HPA023605	IHC,WB,ICC-IF
Anti-MTMR2	HPA049831	IHC	Anti-WFDC2	HPA042302	IHC,WB
Anti-MYBBP1A	HPA005466	IHC,WB,ICC-IF	Anti-ZBTB7B	HPA006811	IHC,WB*,ICC-IF
Anti-NAPEPLD	HPA024338	IHC,WB,ICC-IF	Anti-ZKSCAN3	HPA009637	IHC
Anti-NASP	HPA028136	IHC,WB,ICC-IF	Anti-ZNF131	HPA007023	IHC
Anti-NFIA	HPA006111 <sup>11</sup>	IHC,WB,ICC-IF	Anti-ZNF627	HPA049770	IHC,WB
Anti-NIM1	HPA007695	IHC,WB	Anti-ZNF662	HPA039116	IHC,WB
Anti-NKAIN1	HPA006873	IHC			
Anti-NPSR1	HPA007489 <sup>12</sup>	IHC			
Anti-OR2Z1	HPA048760	IHC			
Anti-OR9K2	HPA015808	IHC			
Anti-OTOP2	HPA024524	IHC			
Anti-PDE4C	HPA048975	IHC,WB			
Anti-PEG10	HPA051038	IHC,ICC-IF			
Anti-PHLPP1	HPA020200	IHC			
Anti-PHTF2	HPA012312	IHC,ICC-IF			
Anti-PKN3	HPA045390	IHC			
Anti-S100A13	HPA019592 <sup>17,18</sup>	IHC,WB			
Anti-PNMA5	HPA044690	IHC			
Anti-PPP1R35	HPA051607	IHC			
Anti-PPR11	HPA023923 <sup>13,14</sup>	IHC,WB			
Anti-PVALB	HPA048536	IHC,WB			
Anti-RAB31	HPA019717 <sup>15</sup>	IHC,WB			
Anti-RAC3	HPA047820	IHC,WB			
Anti-RAD18	HPA008752	IHC,WB,ICC-IF			
Anti-REEP1	HPA058061	IHC			
Anti-RIOK2	HPA005681	IHC,ICC-IF			
Anti-RPS13	HPA005985	IHC			
Anti-S100A1	HPA006462 <sup>16</sup>	IHC,WB			

18. Azimi A, et al. Proteomics analysis of melanoma metastases: association between S100A13 expression and chemotherapy resistance. *Br J Cancer* 2014 May 13; 110(10):2489-2495. Epub 2014 Apr 10.

19. Nguyen VT, et al. Differential epigenetic reprogramming in response to specific endocrine therapies promotes cholesterol biosynthesis and cellular invasion. *Nat Commun* 2015 Nov 27; 6:10044. Epub 2015 Nov 27.

20. Strömberg S et al. Selective expression of Syntaxin-7 protein in benign melanocytes and malignant melanoma. *J Proteome Res* 2009 Apr;8(4):1639-46.

21. Guo Y et al. Regulating the ARNT/TACC3 axis: Multiple approaches to manipulating protein/protein interactions with small molecules. *JACS Chem Biol* 2013 Mar 15; 8(3):626-635. Epub 2012 Dec 26.

# Finding Cancer Biomarkers

## Breast Cancer

Breast cancer is the second most common cancer and by far the most frequent cancer among women. The incidence of breast cancer is increasing steadily, but without a corresponding increase in mortality. If detected at an early stage, the prognosis is relatively good for a patient living in a developed country, with a general five-year survival rate of approximately 85%.

## Breast Cancer and Treatment

Cancer, though often denoted as a singular disease, is truly a multitude of diseases. This understanding has evolved over the years, but many patients are not receiving optimal treatment for their disease. For cancer patients to receive a more individualized treatment, there is still a need for new and better ways to stratify patients. The classical prognostic factors such as stage and grade of the tumor are insufficient for a correct estimation of patient prognosis. Additional information from cancer biomarkers promise to substantially improve this estimation, ultimately leading to a more individualized treatment, thus avoiding both under- and over treatment of patients.

The primary curative treatment for breast cancer patients is surgery, often in combination with adjuvant therapy. However, adjuvant therapy is associated with substantial costs and sometimes severe side effects, and physicians have identified reduction of overtreatment as the major clinical need in breast cancer treatment today. Thus, the stratification of patients into different prognostic categories is of great importance as it may aid physicians in selecting the most appropriate treatment for a given patient.

The majority of breast cancers are hormone receptor responsive, i.e., express the estrogen receptor (ER) and/or the progesteron receptor (PR). Patients with tumors expressing these receptors may receive adjuvant endocrine treatment, such as tamoxifen.

Breast cancers may also express the HER2 protein (human epidermal growth factor receptor 2), and patients with tumors expressing this protein may receive adjuvant therapy with trastuzumab.

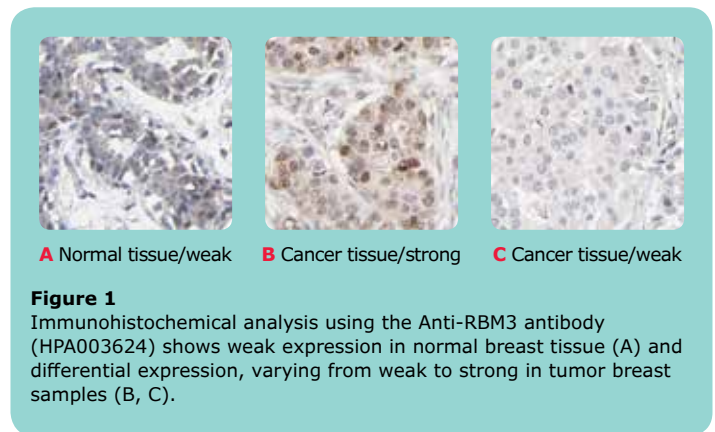
Adjuvant treatment may also consist of chemotherapy or radiation therapy.

## RBM3

The RNA-binding motif protein 3 (RBM3) is an RNA- and DNA-binding protein, whose function has not been fully elucidated. It has been shown that the protein is expressed as an early event in mild hypothermia, and also in other conditions relating to cellular stress, such as glucose deprivation and hypoxia<sup>1</sup>. During stress, RBM3 is thought to protect the cells by aiding in maintenance of protein synthesis needed for survival<sup>1</sup>. Recently, it has also been shown that RBM3 attenuates stem cell-like properties in prostate cancer cells<sup>2</sup>.

RBM3 was identified via the Human Protein Atlas (HPA) as a potential oncology biomarker through the differential expression pattern present in several cancers investigated as part of the HPA project (proteinatlas.org)<sup>3,4</sup>.

The IHC analysis using the Anti-RBM3 antibody HPA003624 showed a weak expression pattern in normal breast tissue, but a stratified pattern in breast cancer tissue (Figure 1). Researchers further investigated the expression in larger breast cancer cohorts and the expression of RBM3 was shown to be associated with a prolonged survival<sup>5</sup>.



**Figure 1**

Immunohistochemical analysis using the Anti-RBM3 antibody (HPA003624) shows weak expression in normal breast tissue (A) and differential expression, varying from weak to strong in tumor breast samples (B, C).

1. Ehlén Å (2011) PhD Thesis: The role of RNA-binding motif 3 in epithelial ovarian cancer: A biomarker discovery approach.
2. Zeng Y et al. (2013) Stress response protein RBM3 attenuates the stem-like properties of prostate cancer cells by interfering with CD44 variant splicing. *Cancer Res.* May 10. [Epub ahead of print]
3. Berglund L et al. (2008) A gene-centric human protein atlas for expression profiles based on antibodies. *Molecular & Cellular Proteomics* 7:2019-2027.
4. Uhlén M et al. (2010) Towards a knowledge-based Human Protein Atlas. *Nat Biotechnol* 28(12):1248-50.

## RBM3 as a Prognostic Biomarker in Breast Cancer

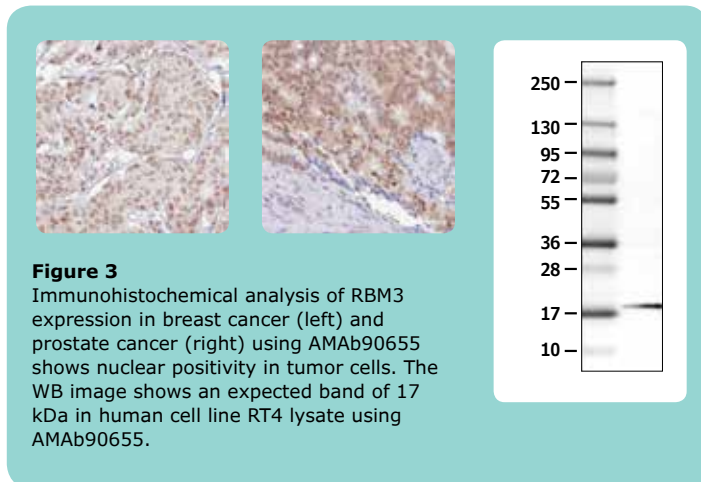
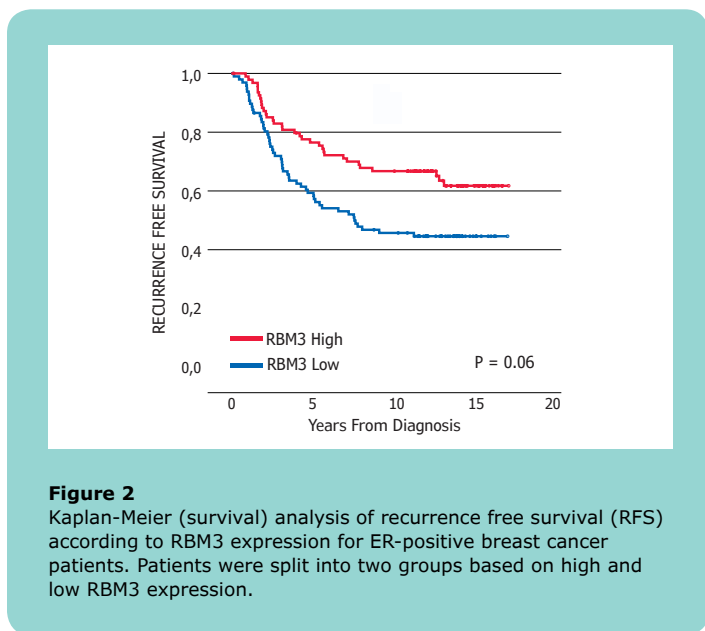
After identification of RBM3 as a potential prognostic biomarker, researchers further investigated the RBM3 protein expression in larger breast cancer cohorts<sup>5</sup>. In a cohort of 500 premenopausal women with stage II invasive breast cancer, RBM3 expression was found to be associated with small, low-grade, estrogen receptor (ER)-positive tumors. When analyzing the subset of ER-positive patients, RBM3 was an independent predictor of recurrence free survival (RFS). As shown in Figure 2, patients with tumors expressing high levels of the RBM3 protein have an improved survival compared to patients with tumors expressing low levels of RBM3.

RBM3 protein expression has further been analyzed in many different patient cohorts from various forms of cancer. Levels of RBM3 expression was found to have a significant connection to patient survival in breast<sup>5</sup>, colon<sup>6</sup>, ovarian<sup>7,8</sup>, testicular, urothelial<sup>9</sup>, and prostate<sup>10</sup> cancer as well as in malignant melanoma<sup>11</sup>.

In conclusion, RBM3 is a marker of good prognosis in breast cancer as well as in several other cancers.

### RBM3 Antibodies

There are two Anti-RBM3 antibodies in the Prestige Antibody product; the Prestige Polyclonal HPA003624 and the Prestige Monoclonal AMAb90655. The monoclonal Anti-RBM3 antibody AMAb90655 has shown excellent specificity in Western Blot analysis of human cell lines, and is routinely used for staining of formalin fixed paraffin embedded tissue in IHC (Figure 3.)



- Jögi A et al. (2009) Nuclear expression of the RNA-binding protein RBM3 is associated with an improved clinical outcome in breast cancer. *Mod Pathol.* Dec;22(12):1564-74.
- Hjelm B et al. (2011) High nuclear RBM3 expression is associated with an improved prognosis in colorectal cancer. *Proteomics Clin Appl.* Dec;5(11-12):624-35
- Ehlén Å et al (2010) Expression of the RNA-binding protein RBM3 is associated with a favourable prognosis and cisplatin sensitivity in epithelial ovarian cancer. *J Transl Med.* Aug 20; 8:78.
- Ehlén Å et al. (2011) RBM3-regulated genes promote DNA integrity and affect clinical outcome in epithelial ovarian cancer. *Transl Oncol.* Aug;4(4):212-21.
- Boman K et al (2013) Decreased expression of RNA-binding motif protein 3 correlates with tumour progression and poor prognosis in urothelial bladder cancer. *BMC Urol.* 2013;13:17
- Jonsson L et al. (2011) High RBM3 expression in prostate cancer independently predicts a reduced risk of biochemical recurrence and disease progression. *Diagn Pathol.* Sep 28;6:91.
- Jonsson L et al. (2011) Low RBM3 protein expression correlates with tumour progression and poor prognosis in malignant melanoma: an analysis of 215 cases from the Malmö Diet and Cancer Study. *J Transl Med.* Jul 21;9:114.

### Granulin

Granulins are a family of secreted, glycosylated peptides that are cleaved from a single precursor protein. Cleavage of the signal peptide produces mature granulin which can be further cleaved into a variety of active peptides. These cleavage products are named granulin A, granulin B, granulin C, etc. Both the peptides and intact granulin protein regulate cell growth. Different members of the granulin protein family may act as inhibitors, stimulators, or have dual actions on cell growth. Granulin family members are important in normal development, wound healing, and tumorigenesis [provided by RefSeq, Jul 2008].

In a paper by Elkabets et al, the role of GRN expression in responding tumor instigation was investigated by studying recruitment of GRN-expressing bone marrow cells into responding tumors in mice<sup>1</sup>. Certain tumors can foster the growth of other tumors or metastatic cells located at distant anatomical sites, which is referred to as tumor instigation. In this study, rigorously growing human breast carcinoma cells were implanted in mice and it was shown that these cells stimulated the outgrowth of otherwise poorly tumorigenic, indolent transformed



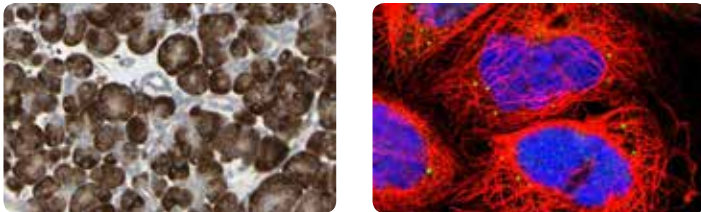
cells. GRN was identified as the most upregulated gene in the instigating bone marrow cells. The GRN expressing cells induced resident fibroblasts to express genes that promoted malignant tumor progression. It was speculated whether anticancer therapies might involve targeting GRN, or the activated GRN expressing cells, and thereby disrupting these cell lines of communication that promote cancer progression.

By using the Anti-GRN antibody HPA028747 in the analysis of tumor tissues from a cohort of breast cancer patients, high GRN expression was shown to correlate with the most aggressive triple-negative, basal-like tumor subtype and reduced patient survival (Figure 1).

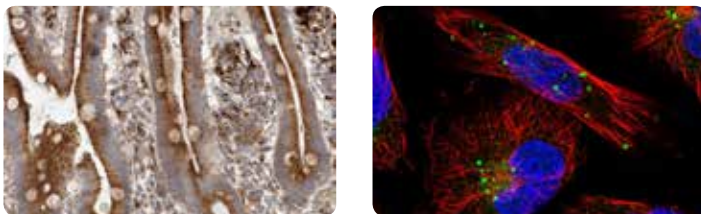
### Granulin Antibodies

In Prestige antibodies' product catalog, there are two polyclonal Anti-GRN antibodies; HPA008763 and HPA028747.

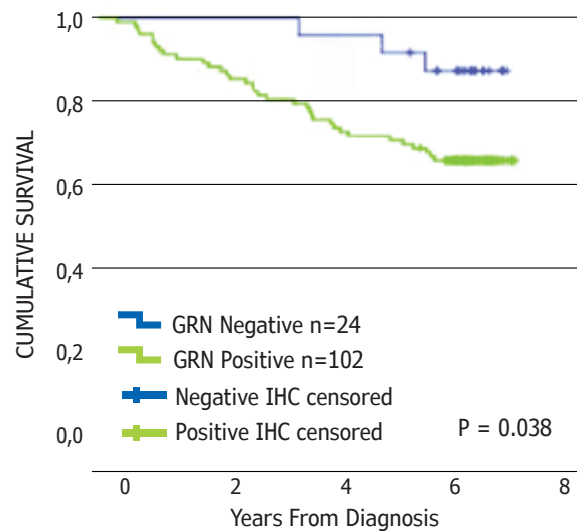
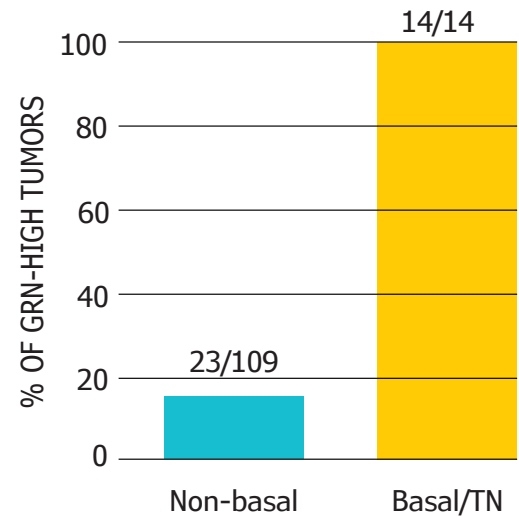
1. Elkabets M et al. Human tumors instigate granulin-expressing hematopoietic cells that promote malignancy by activating stromal fibroblasts in mice. *J Clin Invest* 2011 Feb 1;121(2):784-99.



IHC staining of human pancreas tissue using the Anti-GRN antibody (HPA008763) shows strong cytoplasmic positivity in exocrine glandular cells. ICC-IF shows positivity in vesicles in A-431 cells.

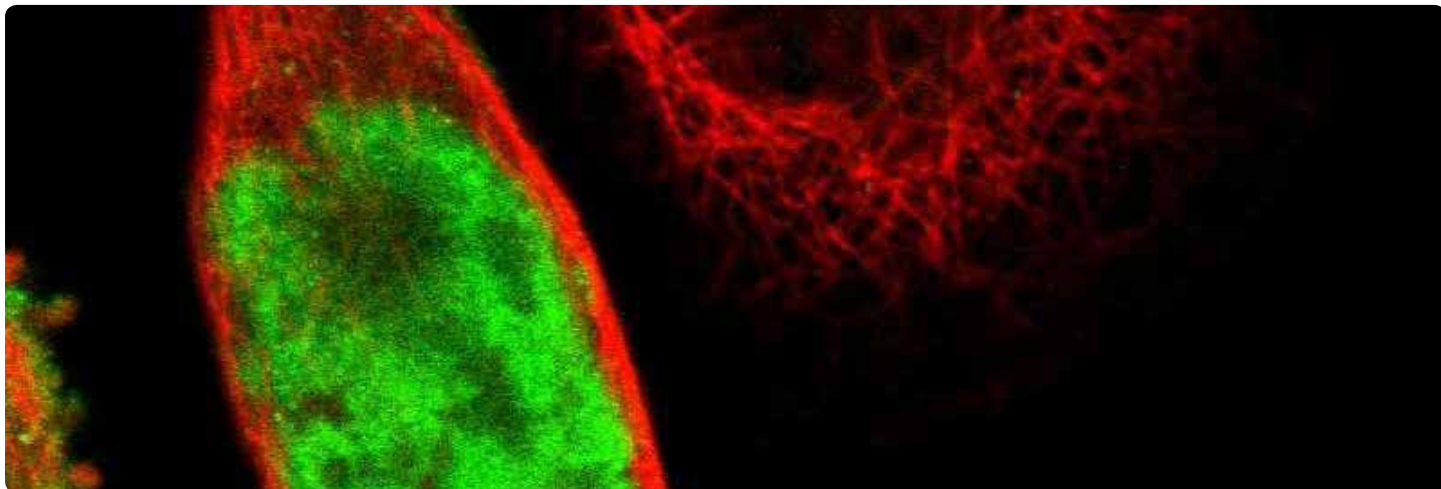


IHC analysis using the Anti-GRN antibody HPA028747 shows strong cytoplasmic positivity in normal duodenum tissue in glandular cells and vesicle positivity in U-251 MG cells.



**Figure 1**

GRN expression was shown to correlate with aggressive tumor subtypes and reduced survival of breast cancer patients using antibody HPA028747. The diagram to the left shows percentage of tumors in each category (Triple-Negative [TN]/basal or nonbasal) that show high GRN positivity and the Kaplan-Meier analysis to the right shows correlation between GRN-positive (green) or GRN-negative (blue) expression and survival.



## Anillin

Anillin is an actin binding protein that is a subunit of microfilaments, one of the cytoskeleton components. Anillin is expressed in most cells and is involved in basic cell functions, e.g. motility, division and signaling. Studies of anillin expression have shown that it is overexpressed in several human tumors.

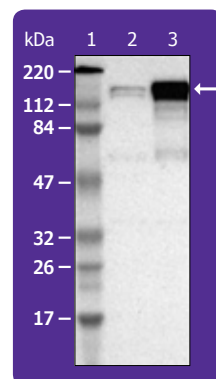
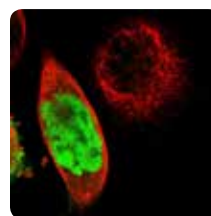
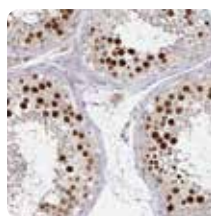
## Anillin as a Treatment Predictive Prognostic Biomarker in Breast Cancer

Anillin expression was analyzed in a patient cohort consisting of 467 samples from patients diagnosed with breast cancer, using the Anti-ANLN antibody HPA005680. Patients with tumors expressing high levels of anillin had a reduced recurrence free survival (RFS) compared to patients with tumors expressing low levels of anillin (Figure 1A). The same association between anillin expression and reduced survival could be seen when analyzing breast cancer specific survival (BCSS, Figure 1B). In a study by O'Leary et al, the prognostic impact of anillin was confirmed by Cox regression analysis. High anillin expression was associated with reduced BCSS and RFS in univariate- as well as in multivariate analysis, adjusted for tumor size and grade, age at diagnosis, nodal-, ER-, PR-, HER2-, and Ki67 status.

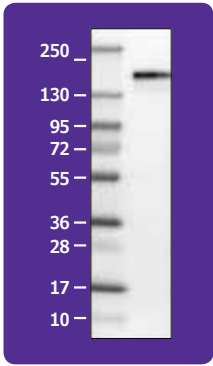
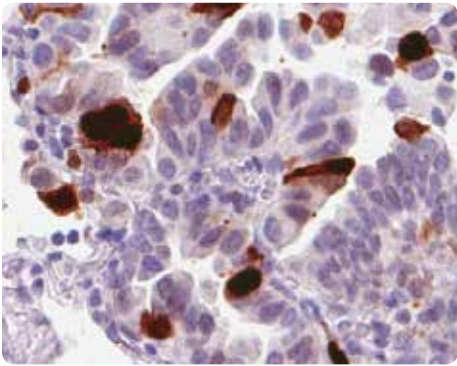
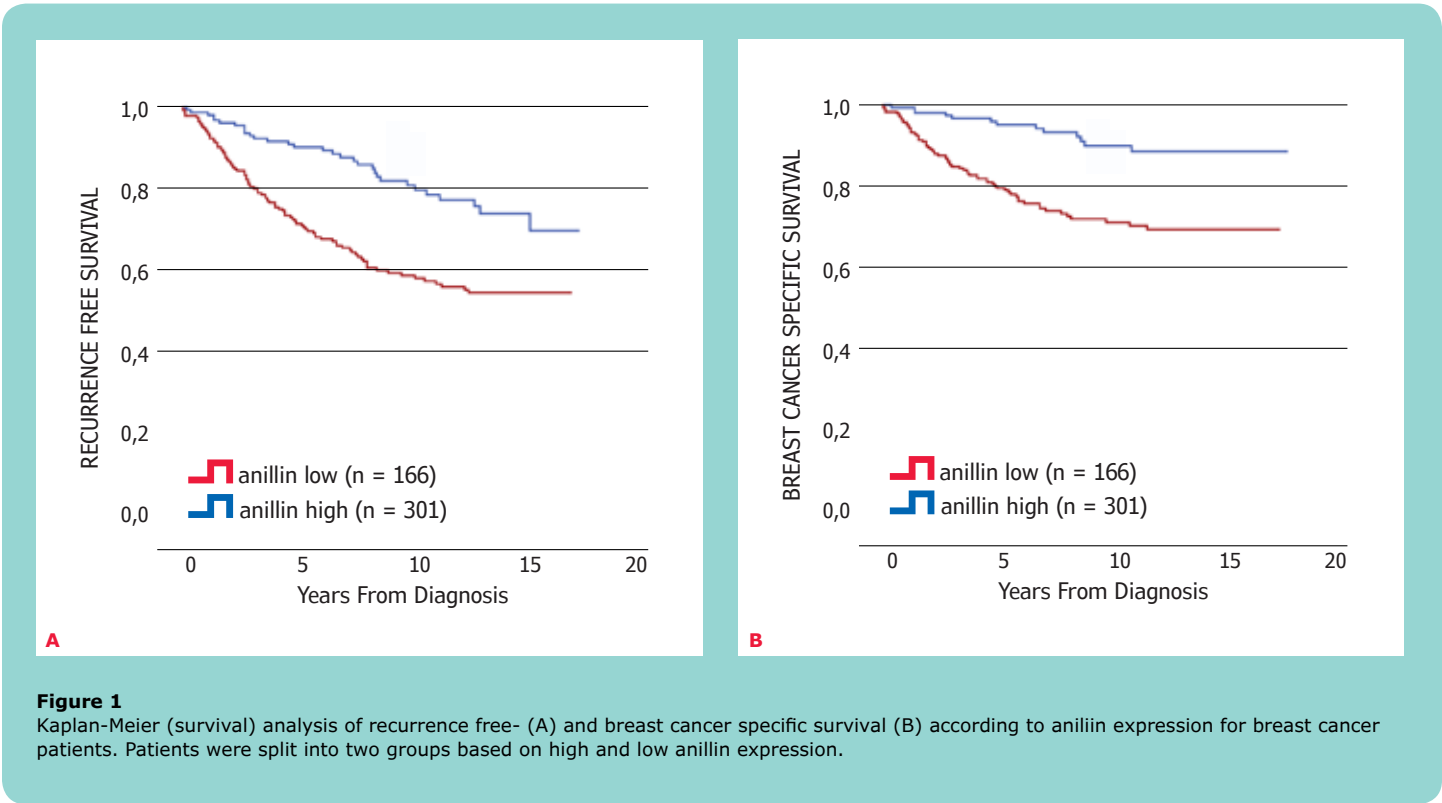
In conclusion, anillin is a marker for poor prognosis in breast cancer.

## Anillin Antibodies

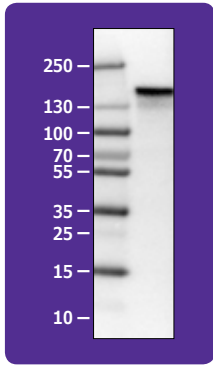
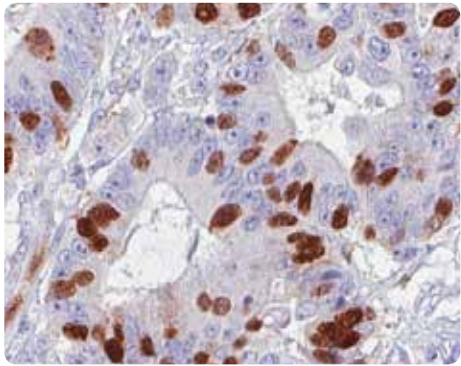
There are three Anti-ANLN antibodies in Prestige antibodies' product; the Prestige Monoclonals AMAb90660 and AMAb90662 and the Prestige Polyclonal HPA005680.



The Anti-ANLN antibody (HPA005680) shows strong nuclear positivity in cells in seminiferous ducts in human testis by IHC. In ICC-IF, nuclei (but not nucleoli) of A-431 cells stain positively and in WB, the antibody detects a band of predicted size in cell lysates of RT-4 and U-251 MG.



Anti-ANLN antibody AMAb90660 shows strong nuclear immunoreactivity in a subset of tumour cells in lung adenocarcinoma and a band of predicted size in human cell line U-251 MG.



AMAb90662 Anti-ANLN antibody shows strong nuclear immunoreactivity in a subset of tumor cells in colorectal cancer and a band of predicted size in human U-251 MG cells.

1. O'Leary PC et al. Systematic antibody generation and validation via tissue microarray technology leading to identification of a novel protein prognostic panel in breast cancer. BMC Cancer. 2013 Apr 2;13:175.

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