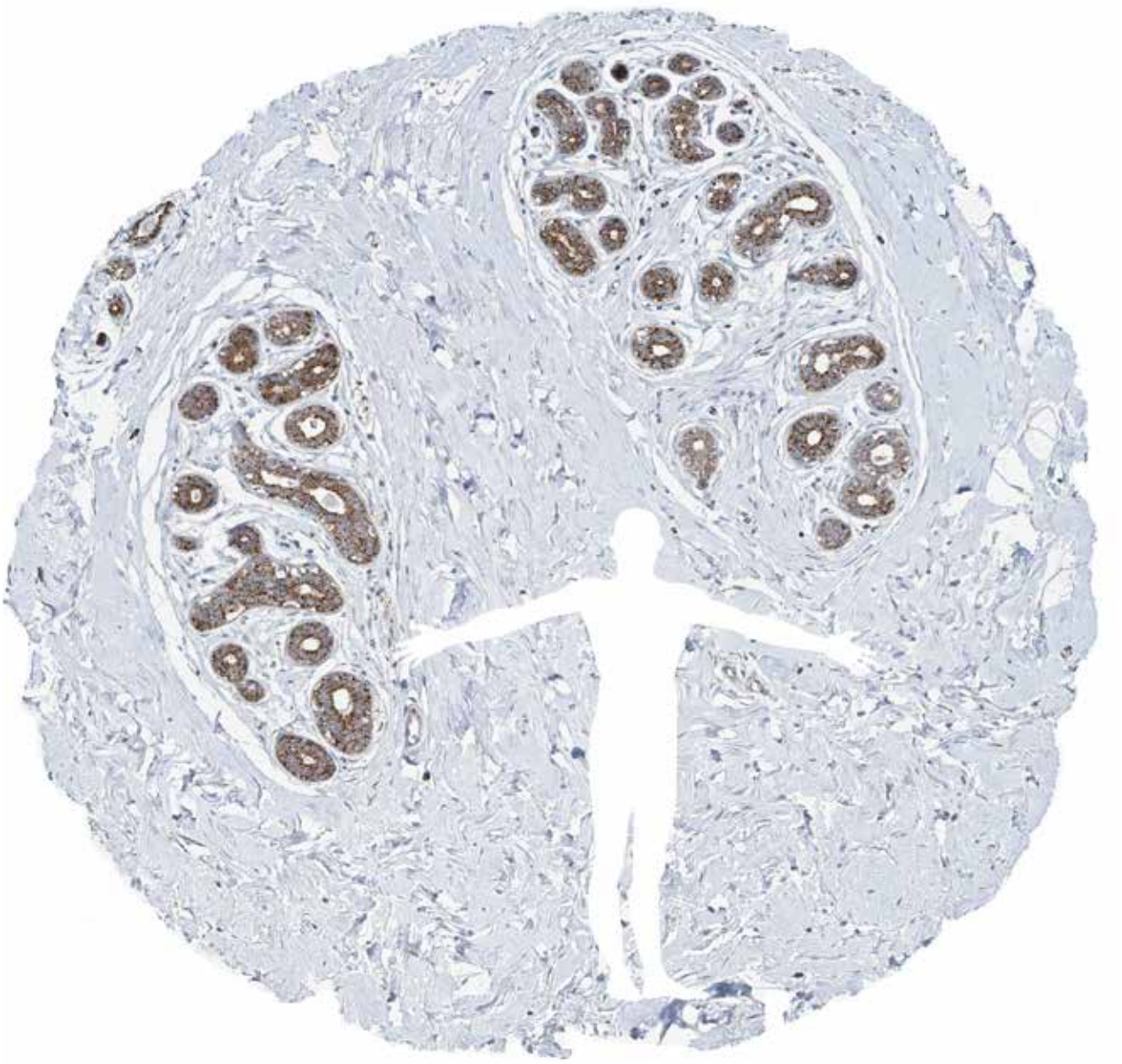

ATLAS ANTIBODIES IN BREAST CANCER RESEARCH

ATLAS ANTIBODIES

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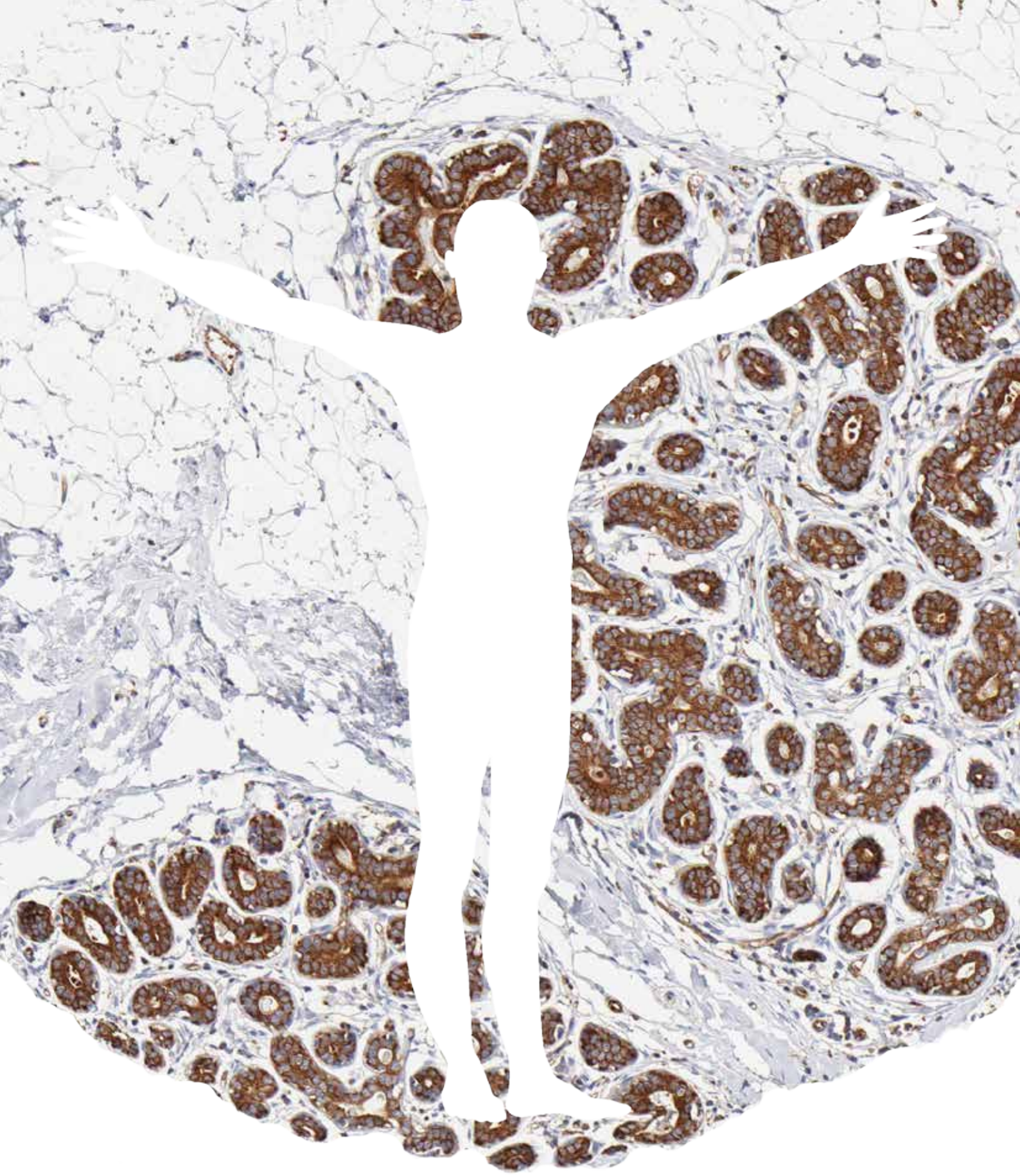
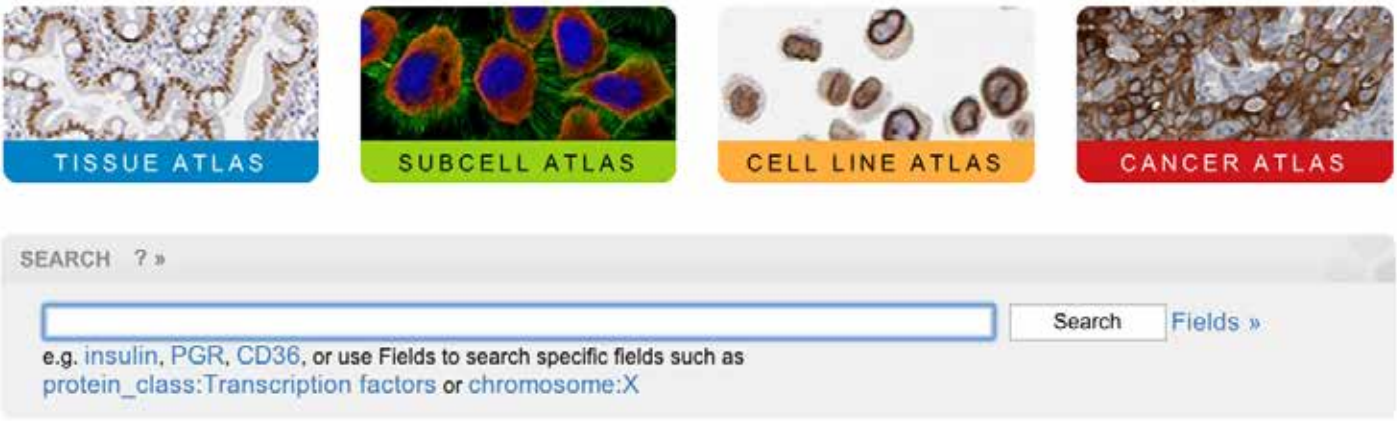


ATLAS ANTIBODIES

THE HUMAN PROTEIN ATLAS



proteinatlas.org

The Human Protein Atlas is Characterizing the Human Proteome

The Human Protein Atlas (HPA) project was initiated in 2003 by Swedish researchers, headed by Professor Mathias Uhlén, and funded by the Knut and Alice Wallenberg foundation[1,2]. It is a unique world leading effort performing systematic exploration of the human proteome using antibodies.

The aim of the HPA project is to present an expression map of the complete human proteome in 2015, with a curated version in 2020. To accomplish this, highly specific Triple A polyclonal antibodies are 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 New Human Protein Atlas, December 2013

The 12th version of the HPA includes antibodies targeting proteins from more than 16,600 human genes, corresponding to 82% of the human proteome. With this update, HPA is now close to the goal of providing profiling data for all human proteins.

In the new version, the extensive amount of data has been divided into four separate 'sub atlases': the Tissue Atlas, the Cancer Atlas, the Subcell Atlas and the Cell Line Atlas. For all proteins represented in the Tissue Atlas, the expression profiles are based on IHC analysis on a large number of human tissues. The presentation of protein expression data in correlation to RNA sequencing data for each gene has now been included. In the Cancer Atlas, differentially expressed genes in several cancers can be studied, while the Subcell Atlas presents subcellular localization by confocal microscopy. Additional information about protein expression in common cell lines is included in the Cell Line Atlas, which has become an appreciated toolbox for research.

Tissue microarrays containing samples from 48 different normal human tissues, 20 different cancer types and 44 different human cell lines are utilized within the project. The 48 normal tissues are present in triplicate samples and represent 82 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 (RNA-Seq) from 27 major different normal tissue types

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 16.621 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.

References:

1. Berglund L *et al.* (2008) A gene-centric human protein atlas for expression profiles based on antibodies. Molecular & Cellular Proteomics 7:2019-2027.

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

Triple A Polyclonals

Triple A Polyclonals - the Building Blocks of HPA

The uniqueness and low cross reactivity of Triple A 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.

Development

The Triple A 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 Triple A 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.

Triple A Polyclonal catalog

Today, there are more than 17,000 Triple A Polyclonals and 2,000 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.

Monoclonal Antibody Development

Atlas Antibodies also provide a selected number of mouse monoclonal antibodies. The 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 monoclonal antibodies 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 monoclonal 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 Atlas Antibodies Monoclonal Antibodies 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 monoclonal antibody is thus supplied with the most relevant characterization data for its specific target.

The product numbers of all Triple A Polyclonals start with "HPA" and of monoclonal antibodies with "AMAb".

Clinical markers (ESR1, HER2, Ki67, PGR)

- established clinical breast cancer markers

Target protein	Product Name	Product Number	Validated Applications
Estrogen receptor	Anti-ESR1	HPA000449	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000450	IHC,WB
Progesteron receptor	Anti-PGR[1]	HPA004751	IHC,ICC-IF
Progesteron receptor	Anti-PGR	HPA008428	IHC
Progesteron receptor	Anti-PGR	HPA017176	IHC
HER2/ERBB2	Anti-ERBB2	HPA001383	IHC,WB
HER2/ERBB2	Anti-HER2	AMAb90627	IHC,WB
Ki67/MKI67	Anti-MKI67[2]	HPA000451	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67[3]	HPA001164	IHC,ICC-IF
Ki67/MKI67	Anti-MKI67	AMAb90870	IHC

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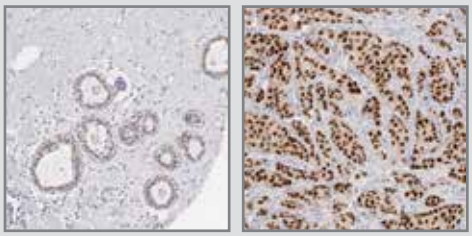
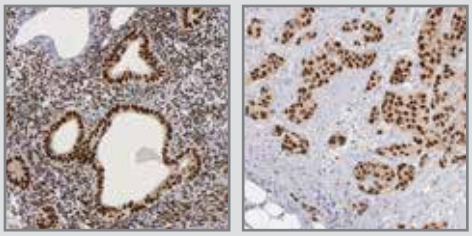
2. Camilleri M *et al.* Neuropeptide S receptor induces neuropeptide expression and associates with intermediate phenotypes of functional gastrointestinal disorders. *Gastroenterology* 2010 Jan;138(1):98-107.e4.

3. 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.

Estrogen receptor



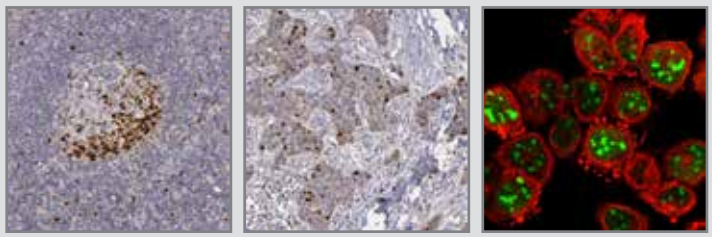
The Anti-ESR1 antibody (HPA000449) shows distinct nuclear positivity in glandular cells in human breast tissue and in tumor cells in breast cancer samples using IHC.



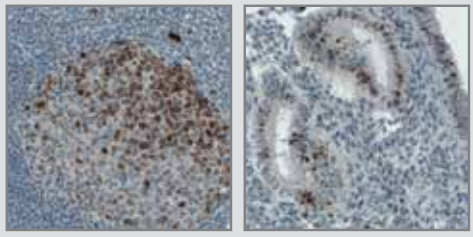
IHC staining using the Anti-ESR1 antibody (HPA000450) shows strong nuclear positivity in glandular and stromal cells of human corpus, uterine tissue and in tumor cells in breast cancer.

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.

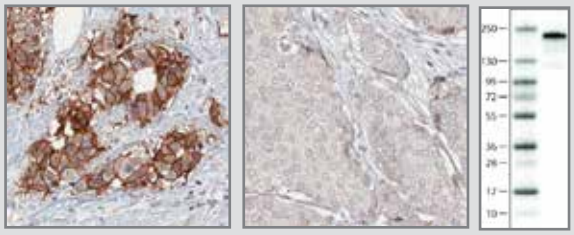


IHC staining of human tonsil tissue using the Anti-MKI67 antibody (HPA001164) shows nuclear staining of reaction center cells. In tumor cells in breast cancer, the staining is mainly nuclear and in U-2OS cells, using ICC-IF, nucleoli show strong positivity.



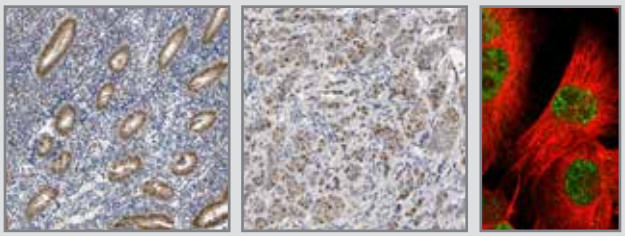
IHC staining of lymph node in human colon shows strong nuclear and nucleolar immunoreactivity in the reaction centrum cells using the monoclonal Anti-MKI67 antibody (AMAb90870). In uterus, nuclear positivity in a subset of glandular cells is shown.

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.

The antibodies are for research use only

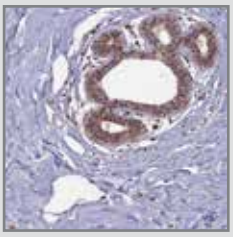
Antibodies used in Breast Cancer Research

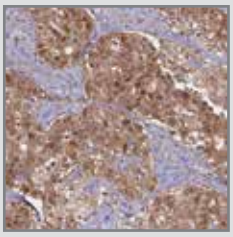
In this section, antibodies are selected either on a reference/ article-basis or on breast cancer relevance for the corresponding target protein.

Target Protein	Product Name	Product Number	Validated Applications
53BP1	Anti-TP53BP1	HPA008788	IHC,ICC-IF
53BP1	Anti-TP53BP1	HPA022133	IHC,WB*,ICC-IF
ACAT1	Anti-ACAT1[1,2]	HPA004428	IHC,WB*,ICC-IF
ACAT1	Anti-ACAT1[2-4]	HPA007569	IHC,WB,ICC-IF
AGR2	Anti-AGR2[5]	HPA007912	IHC,WB
AIB1/NCOA3	Anti-NCOA3	HPA024210	IHC,ICC-IF
Anillin/ANLN	Anti-ANLN	AMAb90660	IHC,WB
Anillin/ANLN	Anti-ANLN	AMAb90662	IHC,WB
Anillin/ANLN	Anti-ANLN[6]	HPA005680	IHC,WB,ICC-IF
ARG1	Anti-ARG1[7]	HPA024006	IHC,WB
ASAH1	Anti-ASAH1[8,9]	HPA005468	IHC,WB
ATR	Anti-ATR	HPA028264	IHC
BAAT1/BRAT1	Anti-BRAT1	HPA029455	IHC
BACH1	Anti-BACH1[10]	HPA003175	IHC,WB,ICC-IF
BAP1	Anti-BAP1	HPA028814	IHC,WB,ICC-IF
BARD1	Anti-BARD1	HPA044864	IHC,ICC-IF
Beta-Catenin	Anti-CTNNB1	HPA029159	IHC,WB*,ICC-IF
Beta-Catenin	Anti-CTNNB1	HPA029160	IHC, IF
BIRC3/API2	Anti-BIRC3[11]	HPA002317	IHC,WB,ICC-IF
BIT1/ PTRH2	Anti-PTRH2[12,13]	HPA012897	IHC,WB,ICC-IF
Blooms Syndrome Prot	Anti-BLM	HPA005689	IHC,ICC-IF
Bmi1	Anti-BMI1	HPA030472	IHC,WB*,ICC-IF
BRCA1	Anti-BRCA1	HPA034966	IHC
BRCA2	Anti-BRCA2	HPA026815	IHC,ICC-IF
BRIP1/FANCJ	Anti-BRIP1	HPA005474	IHC,WB,ICC-IF
C11orf51/ANAPC15	Anti-C11orf51	HPA036596	IHC,WB,ICC-IF
CAR/NR1I3	Anti-NR1I3	HPA051365	IHC,ICC-IF
CASP8	Anti-CASP8	HPA001302	IHC,WB,ICC-IF
CASP8	Anti-CASP8	HPA005688	IHC,WB,ICC-IF
CAXII/CA12	Anti-CA12[14-17]	HPA008773	IHC,WB

* WB both in human and rodent samples

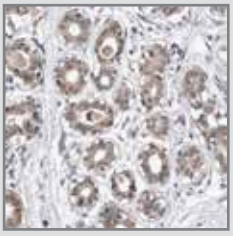
BRCA1

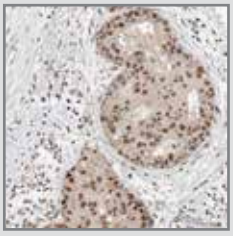




The Anti-BRCA1 antibody (HPA034966) shows positivity in glandular cells in normal human breast tissue and in tumor cells in breast cancer samples using IHC.

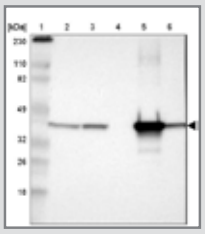
BRCA2

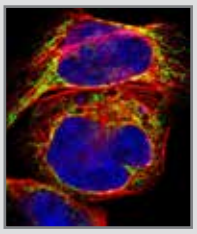




IHC staining using the Anti-BRCA2 antibody (HPA026815) in normal human breast tissue shows positivity in glandular cells. In breast cancer, nuclear staining of tumor cells is shown.

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.

1. 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.

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

15. 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.

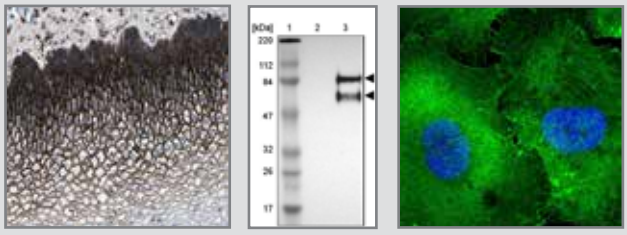
16. Vermeulen *et al.* Differential expression of growth factor receptors and membrane-bound tumor markers for imaging in male and female breast cancer. *PLoS One* 2013;8(1):e53353.

17. 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.

Target Protein	Product Name	Product Number	Validated Applications
CD44	Anti-CD44[18-22]	HPA005785	IHC,WB,ICC-IF
CD82	Anti-CD82	HPA028900	IHC,WB
CDH1	Anti-CDH1	HPA004812	IHC,ICC-IF
CEA/CEACAM5	Anti-CEACAM5	HPA019758	IHC,WB
CHEK2	Anti-CHEK2	HPA001878	IHC,WB
CKB	Anti-CKB	HPA001254	IHC
CRABP2	Anti-CRABP2	HPA004135	IHC,WB,ICC-IF
CTNND1	Anti-CTNND1	HPA015955	IHC,WB*,ICC-IF
CX32/GJB1	Anti-GJB1[23]	HPA010663	IHC,WB
Cyclin E1	Anti-CCNE1	HPA018169	IHC,WB,ICC-IF
cyklin A2	Anti-CCNA2	HPA020626	IHC,WB
Cytokeratin 14/CK14	Anti-KRT14	HPA023040	IHC,WB*,ICC-IF
Cytokeratin 17/CK17	Anti-KRT17[24]	HPA000452	IHC
Cytokeratin 17/CK17	Anti-KRT17	HPA000453	IHC,WB,ICC-IF
DACH2	Anti-DACH2[25]	HPA000258	IHC,ICC-IF
DBC1/KIAA1967	Anti-KIAA1967	HPA019907	IHC,WB*,ICC-IF
DBC1/KIAA1967	Anti-KIAA1967	HPA019943	IHC,ICC-IF
DCAF7	Anti-DCAF7[26]	HPA022962	IHC, WB
Decorin/DCN	Anti-DCN[27,28]	HPA003315	IHC, WB
DIRAS3	Anti-DIRAS3	HPA028483	IHC,WB
DIRAS3	Anti-DIRAS3	HPA028557	IHC,WB
DIRAS3	Anti-DIRAS3	HPA029384	IHC
EGFR	Anti-EGFR	AMAb90816	IHC,WB
EGFR	Anti-EGFR	AMAb90819	WB
EGFR	Anti-EGFR[29]	HPA001200	IHC
EGFR	Anti-EGFR[30]	HPA018530	IHC,WB,ICC-IF
Endoplasmin/ HSP90B1	Anti-HSP90B1[27,31]	HPA003901	IHC,WB,ICC-IF
ERLIN2	Anti-ERLIN2[32,33]	HPA002025	IHC,WB*,ICC-IF
ERFF/C1orf64	Anti-C1orf64[34]	HPA026676	IHC,WB,ICC-IF
FAAH	Anti-FAAH[35]	HPA007425	IHC,ICC-IF
FGFR2	Anti-FGRF2	HPA035305	IHC,WB,ICC-IF
GATA3	Anti-GATA3	HPA029730	IHC,ICC-IF
GATA3	Anti-GATA3	HPA029731	IHC, WB
GCDFP/PIP	Anti-PIP	HPA009177	IHC,WB
GEF-H1	Anti-ARHGEF2[36,37]	HPA017046	IHC,WB
GGH	Anti-GGH[35]	HPA025226	IHC,WB
Granulin	Anti-GRN[38]	HPA008763	IHC,ICC-IF
Granulin	Anti-GRN[38]	HPA028747	IHC,ICC-IF
HIF-1 alpha/HIF1A	Anti-HIF1A[39-42]	HPA001275	IHC,ICC-IF
HJURP	Anti-HJURP[43-45]	HPA008436	IHC,WB,ICC-IF
HMGCL	Anti-HMGCL[2]	HPA004727	IHC,WB
HMGCR	Anti-HMGCR[46]	HPA008338	IHC
HSD17B14	Anti-HSD17B14	HPA021467	IHC,WB,ICC-IF

* WB both in human and rodent samples

CD44



Immunohistochemical staining of human esophagus tissue using Anti-CD44 (HPA005785) shows strong 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.

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Target Protein	Product Name	Product Number	Validated Applications
KLK3/PSA	Anti-KLK3[47,48]	HPA000764	IHC
LSP1	Anti-LSP1	HPA019693	IHC,WB,ICC-IF
MMP2	Anti-MMP2	HPA001939	IHC
MUC1/CA15-3	Anti-MUC1	HPA004179	IHC,WB
MUC1/CA15-3	Anti-MUC1	HPA007235	IHC
MUC1/CA15-3	Anti-MUC1	HPA008855	IHC,ICC-IF
NBN	Anti-NBN	HPA001429	IHC,WB,ICC-IF
NRP1	Anti-NRP1	HPA030278	IHC, WB
Oncostatin M	Anti-OSM[49]	HPA029814	IHC,WB
p63/TP63	Anti-TP63	HPA006288	IHC,ICC-IF
p63/TP63	Anti-TP63	HPA007010	IHC,ICC-IF
PHGDH	Anti-PHGDH[50-52]	HPA021241	IHC,WB*,ICC-IF
PGD	Anti-PGD	HPA031314	IHC,WB*
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,ICC-IF
POLRMT	Anti-POLRMT[53]	HPA006366	IHC
PSPH	Anti-PSPH[50]	HPA020376	IHC,WB
PTMA	Anti-PTMA	HPA047183	IHC,ICC-IF
PTTG1	Anti-PTTG1	HPA008890	IHC,ICC-IF
RAP80/UIMC1	Anti-UIMC1	HPA037503	IHC,WB
RAP80/UIMC1	Anti-UIMC1	HPA037504	IHC,WB,ICC-IF
REST	Anti-REST[54,55]	HPA006079	IHC,ICC-IF
RBM3	Anti-RBM3[56,57]	HPA003624	IHC,WB*,ICC-IF
RBM3	Anti-RBM3[58-65]	AMAb90655	IHC,WB
RRBP1	Anti-RRBP1[66]	HPA009026	IHC,ICC-IF
rs4973768/SLC4A7	Anti-SLC4A7	HPA035857	IHC
SIX1	Anti-SIX1[67-74]	HPA001893	IHC,WB,ICC-IF
SNCG	Anti-SNCG	HPA014404	IHC,WB
STK11	Anti-STK11	HPA017254	IHC,WB,ICC-IF
SURVIvin/BIRC5	Anti-BIRC5	HPA002830	IHC,WB,ICC-IF
T-STAR/KHDRBS3	Anti-KHDRBS3[75,76]	HPA000500	IHC
Tenascin C/TNC	Anti-TNC[77-79]	HPA004823	IHC,WB
TFF1	Anti-TFF1[80-82]	HPA003425	IHC,WB
THBD	Anti-THBD	HPA002982	IHC
THEM2/ACOT13	Anti-ACOT13	HPA019881	IHC,WB*,ICC-IF
TOP2A	Anti-TOP2A	HPA006458	IHC,WB,ICC-IF
TOP2A	Anti-TOP2A	HPA026773	IHC,ICC-IF
UGT8	Anti-UGT8[83]	HPA014405	IHC,ICC-IF
ULBP1	Anti-ULBP1[84]	HPA007547	IHC
ZNF703	Anti-ZNF703[32]	HPA023930	IHC,ICC-IF

* WB both in human and rodent samples

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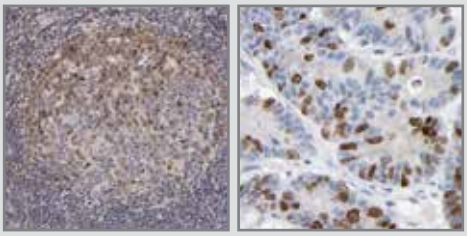
Antibodies against gene products in MammaPrint, Oncotype, EndoPredict and uPA tests

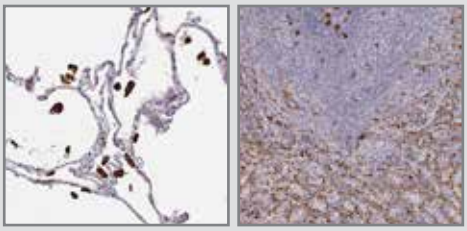
This section presents antibodies in Atlas Antibodies´ product catalog against gene products included in the diagnostic MammaPrint, EndoPredict, Oncotype and uPA tests. MammaPrint is a gene expression profile test based on the Amsterdam 70-gene breast cancer gene signature marketed by Agendia. It is a 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.

BIRC5/Survivin



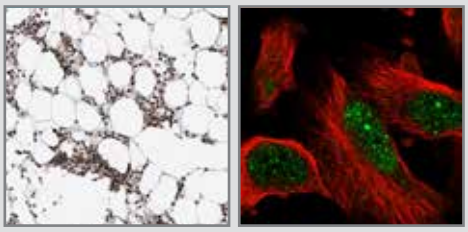
The Anti- BIRC5 antibody (HPA002830) shows nuclear positivity in germinal center cells in human tonsil tissue and in tumor cells in colorectal cancer using IHC.

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

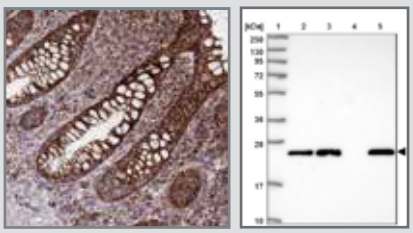


IHC staining of human bone marrow using the Anti-DTL antibody (HPA028016) shows strong nuclear positivity in bone marrow poietic cells. By ICC-IF, staining of nucleus in U-251 MG cells is detected.

Target Protein	Product Name	Product Number	Validated Applications
AURKA/STK15	Anti-AURKA	HPA002636	IHC,WB
AZGP1	Anti-AZGP1	HPA012582	IHC,WB
BAG1	Anti-BAG1	HPA018121	IHC,ICC-IF
BIRC5/Survivin	Anti-BIRC5	HPA002830	IHC,WB,ICC-IF
CD68/Macrosialin	Anti-CD68	HPA048982	IHC
CDCA7	Anti-CDCA7[1,2]	HPA005565	IHC,WB,ICC-IF
CMC2/C16orf61	Anti-CMC2	HPA006871	IHC
DHCR7	Anti-DHCR7	HPA044280	IHC,WB
DHX58/LGP2	Anti-DHX58	HPA018670	IHC,WB,ICC-IF
DHX58/LGP2	Anti-DHX58	HPA019570	IHC
DIAPH3	Anti-DIAPH3	HPA032152	IHC,WB*
DTL	Anti-DTL[3]	HPA028016	IHC,WB,ICC-IF
ECI2/PECI	Anti-ECI2	HPA022130	IHC,WB,ICC-IF
EGLN1/PHD2	Anti-EGLN1[4]	HPA022129	IHC,ICC-IF
ESM1	Anti-ESM1	HPA036660	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000449	IHC,WB
Estrogen receptor	Anti-ESR1	HPA000450	IHC,WB
Exostosin-1	Anti-EXT1	HPA044394	IHC,WB
FGF18	Anti-FGF18	HPA018795	IHC,WB,ICC-IF
GMPS	Anti-GMPS	HPA050682	IHC
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-ERBB2	HPA001383	IHC,WB
HER2/ERBB2	Anti-HER2	AMAb90627	IHC,WB
HRASLS	Anti-HRASLS	HPA051179	IHC
IL6ST/GP130	Anti-IL6ST[5]	HPA010558	IHC
JHDM1D/KDM7A	Anti-JHDM1D	HPA012114	IHC,ICC-IF

* WB both in human and rodent samples

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.

1. 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.

2. 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.

3. Karaayvaz M *et al.* Prognostic significance of miR-215 in colon cancer. *Clin Colorectal Cancer* 2011 Dec;10(4):340-7.

4. Bozóky B *et al.* Novel signatures of cancer-associated fibroblasts. *Int J Cancer* 2013 Jan 15.

5. 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.
S Alterations in Breast Cancer from Women Treated with Neoadjuvant Chemotherapy. *PLoS One* 2013;8(3):e60576.

Target Protein	Product Name	Product Number	Validated Applications
Ki67/MKI67	Anti-MKI67[6]	HPA000451	IHC,ICC-IF
KI67/MKI67	Anti-MKI67[7]	HPA001164	IHC,ICC-IF
KI67/MKI67	Anti-MKI67	AMAb90870	IHC
LIN9	Anti-LIN9	HPA030241	IHC,ICC-IF
LPCAT/AYTL2	Anti-LPCAT1	HPA012501	IHC,WB
LPCAT/AYTL2	Anti-LPCAT1[8]	HPA022268	IHC,WB,ICC-IF
LYRIC	Anti-MTDH[9]	HPA015104	IHC,WB,ICC-IF
LYRIC	Anti-MTDH[10]	HPA010932	IHC,WB*,ICC-IF
LYRIC	Anti-MTDH	AMAb90762	IHC,WB
LYRIC	Anti-MTDH	AMAb90763	IHC,WB
Matrix Gla protein	Anti-MGP[11]	HPA013949	IHC
MCM6	Anti-MCM6	HPA004818	IHC,WB*,ICC-IF
MELK/PK38	Anti-MELK	HPA017214	IHC,ICC-IF
MMP9	Anti-MMP9	HPA001238	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
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

* WB both in human and rodent samples

6. Pohler E *et al.* Haploinsufficiency for AAGAB causes clinically heterogeneous forms of punctate palmoplantar keratoderma. *Nat Genet* 2012 Oct 14;44(11):1272-6.

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.

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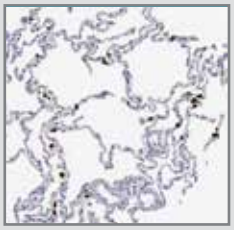
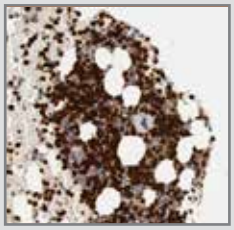
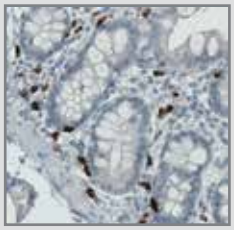
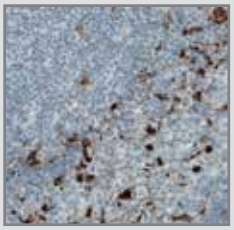
MMP9





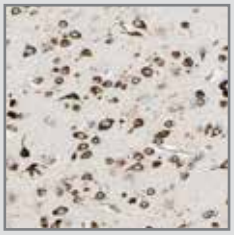
IHC staining of human lung tissue using the Anti-MMP9 antibody (HPA001238) shows strong nuclear positivity in macrophages and in bone marrow poietic cells in bone marrow tissue.

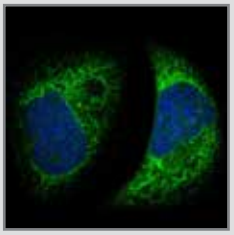




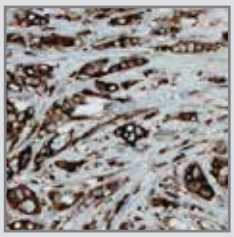
Monclonal Anti-MMP9 antibodies show strong cytoplasmic positivity in a subset of lymphoid cells in duodenum (AMAb90805) and in human tonsil tissue (AMAb90804).

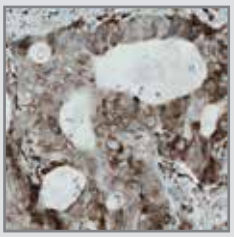
LYRIC/MTDH





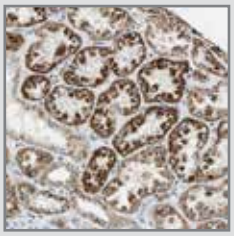
IHC staining using the Anti-MTDH antibody (HPA010932) shows strong cytoplasmic positivity in neuronal cells in human cerebral cortex tissue.
In ICC-IF in A-431 cell line, the antibody stains endoplasmic reticulum.

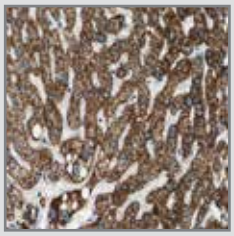




IHC staining using the monclonal Anti-MTDH antibody (AMAb90762) shows strong cytoplasmic reactivity in tumor cells from breast and colorectal cancer samples.

P5C dehydrogenase/ALDH4A1





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

Target Protein	Product Name	Product Number	Validated Applications
PITRM1/MP1	Anti-PITRM1	HPA003232	IHC
PITRM1/MP1	Anti-PITRM1	HPA006753	IHC,WB,ICC-IF
PITRM1/MP1	Anti-PITRM1	HPA006754	IHC,WB*,ICC-IF
PLAU/UPA	Anti-PLAU	HPA008719	IHC,WB
PRC1	Anti-PRC1	HPA034521	IHC,ICC-IF
Progesteron receptor	Anti-PGR[12]	HPA004751	IHC,ICC-IF
Progesteron receptor	Anti-PGR	HPA008428	IHC
Progesteron receptor	Anti-PGR	HPA017176	IHC
QSOX2/QSCN6L1	Anti-QSOX2	HPA012716	IHC,WB,ICC-IF
RBBP8	Anti-RBBP8	HPA039890	IHC, WB
RECQL5	Anti-RECQL5	HPA029970	IHC,ICC-IF
RECQL5	Anti-RECQL5	HPA029971	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[13]	HPA012047	IHC,WB*,ICC-IF
SERPINE1/PAI1	Anti-SERPINE1	HPA050039	IHC
SLC2A3/GLUT3	Anti-SLC2A3	HPA006539	IHC
Stanniocalcin-2	Anti-STC2	HPA045372	IHC, WB, IF
STK32B	Anti-STK32B	HPA015820	IHC,ICC-IF
TGFB3	Anti-TGFB3	HPA027923	IHC,WB
TMEM74B/C20orf46	Anti-TMEM74B	HPA045213	IHC
TSPYL5	Anti-TSPYL5	HPA031347	IHC
UCHL5	Anti-UCHL5	HPA005908	IHC,ICC-IF
VEGFR-1	Anti-FLT1[14]	HPA011740	IHC,ICC-IF
VEGFR-1	Anti-FLT1	HPA014290	IHC,ICC-IF
VEGFR-1	Anti-FLT1	AMAb90703	IHC
VEGFR-1	Anti-FLT1	AMAb90704	IHC,WB
WISP1	Anti-WISP1	HPA007121	IHC,ICC-IF

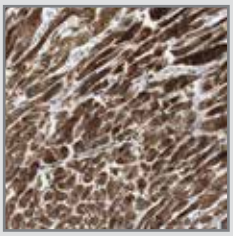
* WB both in human and rodent samples

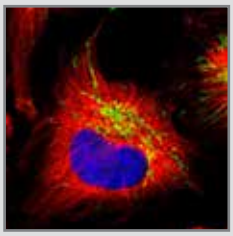
12. Pereira CB *et al.* Prognostic and Predictive Significance of MYC and KRAS Alterations in Breast Cancer from Women Treated with Neoadjuvant Chemotherapy. *PLoS One* 2013;8(3):e60576.

13. 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.

14. 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.

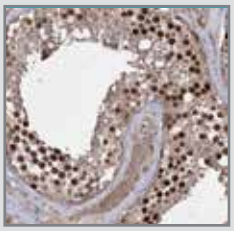
PITRM1/MP1

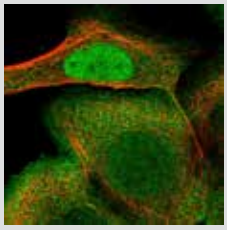




The Anti- PITRM1 antibody (HPA006753) shows strong cytoplasmic positivity in myocytes in human heart muscle using IHC.
ICC-IF staining of human cell line U-251 MG shows positivity in mitochondria.

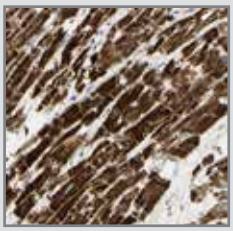
PRC1

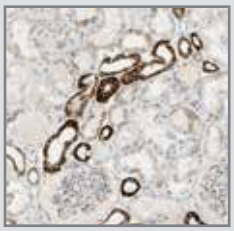


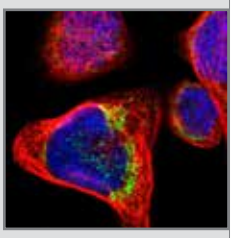


IHC staining of human testis tissue using the Anti-PRC1 antibody (HPA034521) shows strong nuclear positivity in cells of seminiferus ducts. ICC-IF shows staining of nucleus, plasma membrane and microtubules in A-431 cells.

SCOT/OXCT1







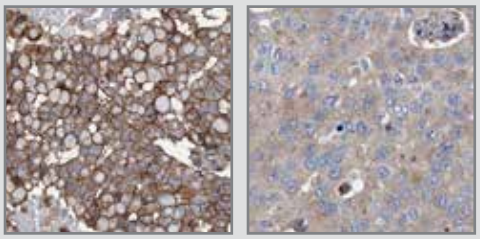
IHC staining of human heart muscle and kidney by Anti-OXCT1 antibody (HPA028016) shows strong cytoplasmic positivity in myocytes and cells in tubules, respectively. ICC-IF shows staining of mitochondria in A431 cells.

Antibodies identified in the Human Protein Atlas

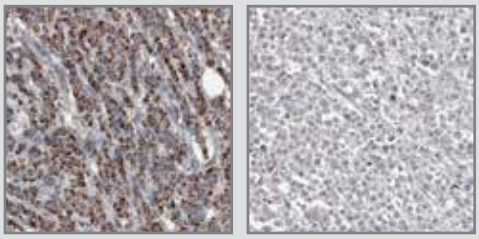
- showing differential IHC staining patterns in breast cancer samples

Product Name	Product Number	Validated Applications
Anti-AAMDC	HPA037918	IHC,WB
Anti-AAMDC	HPA037919	IHC
Anti-ABCG4	HPA040312	IHC,ICC-IF
Anti-AC114947.1	HPA007695	IHC,WB,ICC-IF
Anti-AC145676.2	HPA023993	IHC,WB
Anti-ACSF2	HPA024693	IHC,WB
Anti-ADAMTS13	HPA042014	IHC,WB
Anti-AGR3	HPA053942	IHC
Anti-AIF1L	HPA020522	IHC,WB
Anti-AJUBA	HPA006171	IHC, WB
Anti-ALDH1A3	HPA046271	IHC,WB
Anti-ANKRD46	HPA013758	IHC,WB
Anti-ASB6	HPA004341	IHC,WB,ICC-IF
Anti-ATF6	HPA005935	IHC
Anti-ATP6V1B2	HPA008147	IHC,WB*,ICC-IF
Anti-AVPR2	HPA046678	IHC
Anti-BCL9	HPA020274	IHC
Anti-BTG4	HPA038478	IHC
Anti-C10orf116	HPA026810	IHC,WB
Anti-C10orf54	HPA007968	IHC,WB,ICC-IF
Anti-C12orf76	HPA039713	IHC,WB
Anti-C17orf85	HPA008959	IHC
Anti-C1ORF195	HPA045811	IHC,ICC-IF
Anti-C2orf68	HPA051143	IHC
Anti-C5orf25	HPA037889	IHC,WB
Anti-CAPN8	HPA021480	IHC,WB
Anti-CCDC144NL	HPA023457	IHC,WB
Anti-CCDC170	HPA027185	IHC,WB
Anti-CCDC170	HPA027121	IHC,WB
Anti-CDK6	HPA002637	IHC,WB*,ICC-IF
Anti-CLDN3	HPA014361	IHC
Anti-CPNE2	HPA041132	IHC,WB
Anti-CRABP2	HPA004135	IHC,WB,ICC-IF
Anti-CTNND2	HPA015077	IHC
Anti-CXorf67	HPA006128	IHC,WB
Anti-CYP4X1	HPA017661	IHC
Anti-DACH1	HPA012672	IHC,ICC-IF
Anti-DBF4	HPA051589	IHC
Anti-DCHS1	HPA050246	IHC
Anti-DCLK1	HPA015655	IHC
Anti-DECR2	HPA047631	IHC
Anti-DOM3Z	HPA046708	IHC
Anti-DUSP26	HPA018221	IHC,WB
Anti-ECD	HPA006465	IHC,WB,ICC-IF
Anti-EFHD1	HPA049331	IHC,WB,ICC-IF
Anti-EPHA6	HPA007397	IHC
Anti-FAM101B	HPA030879	IHC
Anti-FAM189A1	HPA009410	IHC
Anti-FKBP7	HPA008707	IHC,WB*,ICC-IF
Anti-FMN2	HPA004937	IHC
Anti-G6PC	HPA052324	IHC
Anti-GABRD	HPA044371	IHC,WB
Anti-GAK	HPA027463	IHC,ICC-IF

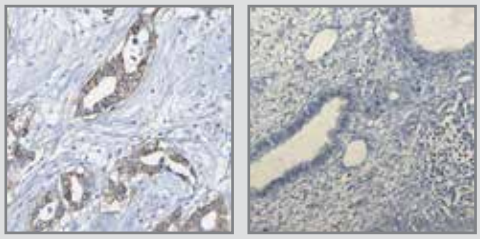
* WB both in human and rodent samples



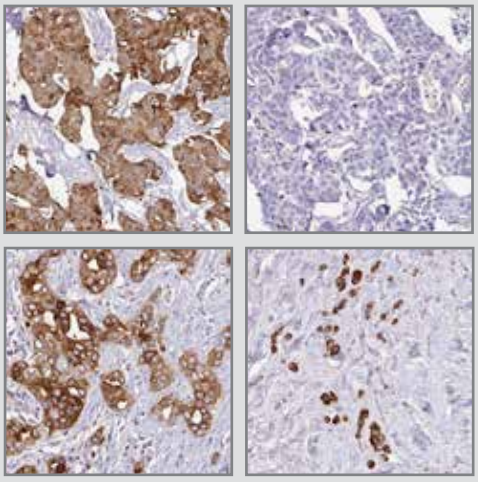
IHC analysis using Anti-KLHL26 antibody (HPA023074) shows a varying membranous/cytoplasmic staining pattern in breast tumor samples from different patients.



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.



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

Product Name	Product Number	Validated Applications
Anti-GCM1	HPA011343	IHC
Anti-GLB1L3	HPA039916	IHC
Anti-GLDC	HPA002318	IHC,WB*
Anti-GLYATL1	HPA039501	IHC,WB
Anti-GTF3A	HPA007990	IHC,ICC-IF
Anti-HIPK2	HPA007611	IHC,ICC-IF
Anti-HMGCS1	HPA036913	IHC,WB,ICC-IF
Anti-HMGCS2	HPA027423	IHC,WB
Anti-HMGCS2	HPA027442	IHC,WB
Anti-IFITM3	HPA004337	IHC,WB
Anti-IRX2	HPA054669	IHC,WB
Anti-ISYNA1	HPA007931	IHC
Anti-ISYNA1	HPA008232	IHC,WB
Anti-ITGA3	HPA008572	IHC
Anti-ITGBL1	HPA005676	IHC,WB
Anti-ITIH6	HPA000506	IHC
Anti-KLHL2	HPA051637	IHC
Anti-KLHL26	HPA023074	IHC,WB
Anti-KRT31	HPA049550	IHC
Anti-KRT32	HPA040330	IHC
Anti-KRTAP9-3	HPA042482	IHC
Anti-LASP1[1]	HPA012072	IHC,WB*,ICC-IF
Anti-LGR6	HPA008556	IHC
Anti-LRRIQ4	HPA036706	IHC
Anti-MAGEB1	HPA002820	IHC
Anti-MANSC4	HPA039454	IHC,WB
Anti-MROH2B	HPA059457	IHC
Anti-MRS2	HPA017642	IHC,WB
Anti-MSTO1	HPA005914	IHC
Anti-MTMR2	HPA049831	IHC
Anti-MYBBP1A	HPA005466	IHC,WB,ICC-IF
Anti-NAPEPLD	HPA024338	IHC,WB,ICC-IF
Anti-NASP	HPA028136	IHC,WB,ICC-IF
Anti-NFIA	HPA006111	IHC,WB*,ICC-IF
Anti-NKAIN1	HPA006873	IHC
Anti-NPSR1[2]	HPA007489	IHC,ICC-IF
Anti-OR2Z1	HPA048760	IHC
Anti-OR9K2	HPA015808	IHC
Anti-OTOP2	HPA024524	IHC
Anti-PDE4C	HPA048975	IHC,WB
Anti-PEG10	HPA051038	IHC,ICC-IF
Anti-PHLDA2	HPA003994	IHC
Anti-PHLPP1	HPA020200	IHC
Anti-PHTF2	HPA012312	IHC
Anti-PKN3	HPA045390	IHC
Anti-PNMA5	HPA044690	IHC,ICC-IF
Anti-PPP1R35	HPA051607	IHC
Anti-PPR11	HPA023923	IHC,WB,ICC-IF
Anti-PVALB	HPA048536	IHC
Anti-RAB31[3]	HPA019717	IHC,WB*
Anti-RAC3	HPA047820	IHC,WB
Anti-RAD18	HPA008752	IHC,WB
Anti-REEP1	HPA058061	IHC

Product Name	Product Number	Validated Applications
Anti-RIOK2	HPA005681	IHC,ICC-IF
Anti-RNF152	HPA015733	IHC,WB
Anti-RPS13	HPA005985	IHC
Anti-S100A1	HPA006462	IHC,WB,ICC-IF
Anti-S100A13	HPA019592	IHC,WB*
Anti-S100A14	HPA027613	IHC,ICC-IF
Anti-S100A7	HPA006997	IHC,ICC-IF
Anti-SGK196	HPA013321	IHC,WB,ICC-IF
Anti-SH3BGRL	HPA051248	IHC,WB
Anti-SHROOM1	HPA037690	IHC
Anti-SLC16A7	HPA005911	IHC,WB
Anti-SLC39A6	HPA042377	IHC,WB
Anti-SPAG1	HPA023748	IHC,ICC-IF
Anti-SQLE	HPA018038	IHC,WB
Anti-SRPRB	HPA011173	IHC,WB
Anti-SSSCA1	HPA039789	IHC,WB*,ICC-IF
Anti-STAG3	HPA049106	IHC,WB,ICC-IF
Anti-STARD6	HPA042583	IHC,IF
Anti-STX7[4]	HPA001467	IHC,WB*,ICC-IF
Anti-TACC3	HPA005781	IHC,WB
Anti-TAPBP	HPA007066	IHC
Anti-TBC1D9	HPA000262	IHC,ICC-IF
Anti-TCTE3	HPA046156	IHC
Anti-TGFBI	HPA017019	IHC
Anti-TMEM110-MUSTN1	HPA051855	IHC
Anti-TMEM222	HPA016579	IHC,ICC-IF
Anti-TMEM47	HPA046658	IHC
Anti-TMEM68	HPA018216	IHC,ICC-IF
Anti-TPX2	HPA005487	IHC,WB,ICC-IF
Anti-TTLL12	HPA003054	IHC,WB
Anti-UBE20	HPA023605	IHC,WB*
Anti-WFDC2	HPA042302	IHC
Anti-WNT3A	HPA050514	IHC
Anti-ZBTB7B	HPA006811	IHC,WB*,ICC-IF
Anti-ZKSCAN3	HPA009637	IHC,ICC-IF
Anti-ZNF131	HPA007023	IHC
Anti-ZNF627	HPA049770	IHC,WB
Anti-ZNF662	HPA039116	IHC,WB

* WB both in human and rodent samples

1. Ngan E *et al.* A complex containing LPP and α-Actinin mediates TGF β-induced migration and invasion of ErbB2-expressing breast cancer cells. *J Cell Sci* 2013 May 1; 126(0 9):1981-1991. Epub 2013/02/27.

2. 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.

3. Bozóky B *et al*. Novel signatures of cancer-associated fibroblasts. *Int J Cancer* 2013 Jan 15.

4. 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.

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.

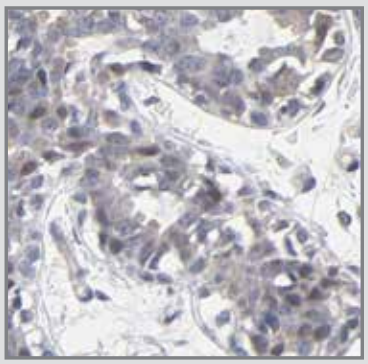
Adjuvant treatment may also consist of chemotherapy or radiation therapy.

RBM3

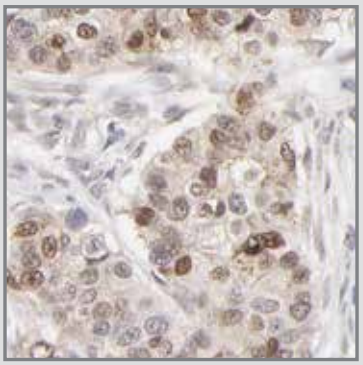
The RNA-binding motif protein 3 (RBM3) is an RNA- and DNA-binding protein, whose function has not been fully elucidated. It has been shown that the protein is expressed as an early event in mild hypothermia, and also in other conditions relating to cellular stress, such as glucose deprivation and hypoxia[1].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

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)[3,4].

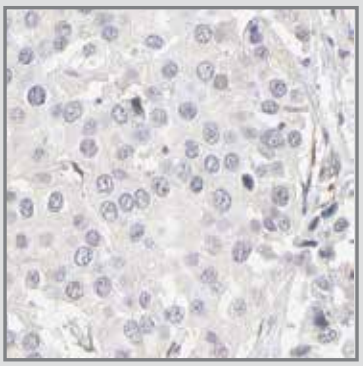
The IHC analysis using the Anti-RBM3 antibody HPA003624 showed a weak expression pattern in normal breast tissue, but a stratified pattern in breast cancer tissue (Figure 1). Researchers further investigated the expression in larger breast cancer cohorts and the expression of RBM3 was shown to be associated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



A Normal tissue - weak



B Cancer tissue - strong



C Cancer tissue - weak

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[5]. 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[5], colon[6], ovarian[7,8], testicular, urothelial[9], and prostate[10] cancer as well as in malignant melanoma[11].

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

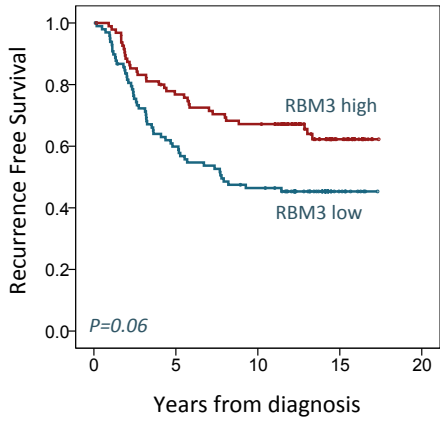


Figure 2
Kaplan-Meier (survival) analysis of recurrence free survival (RFS) according to RBM3 expression for ER-positive breast cancer patients. Patients were split into two groups based on high and low RBM3 expression.

RBM3 antibodies

There are two Anti-RBM3 antibodies in Atlas Antibodies´ product catalog; the rabbit polyclonal antibody HPA003624 and the mouse monoclonal antibody 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.)

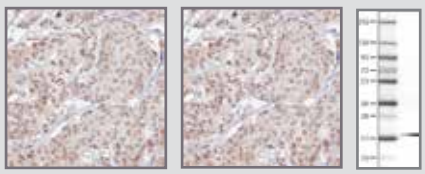


Figure 3
Immunohistochemical analysis of RBM3 expression in breast cancer (left) and prostate cancer (right) using AMAb90655 shows nuclear positivity in tumor cells. The WB image shows an expected band of 17 kDa in human cell line RT4 lysate using AMAb90655.

5. 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.

6. 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

7. 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.

8. 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.

9. 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

10. 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.

11. 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

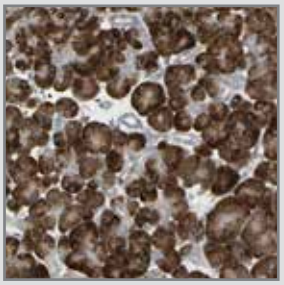
Granulins are a family of secreted, glycosylated peptides that are cleaved from a single precursor protein. Cleavage of the signal peptide produces mature granulin which can be further cleaved into a variety of active peptides. These cleavage products are named granulin A, granulin B, granulin C, etc. 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 recrution of GRN-expressing bone marrow cells into responding tumors in mice[1]. 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.

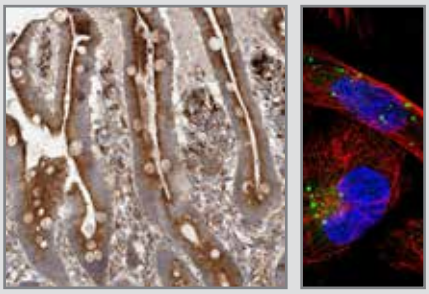
By using the Anti-GRN antibody HPA028747 in the analysis of tumor tissues from a cohort of breast cancer patients, high GRN expression was shown to correlate with the most aggressive triple-negative, basal-like tumor subtype and reduced patient survival (Figure 1).

Granulin antibodies

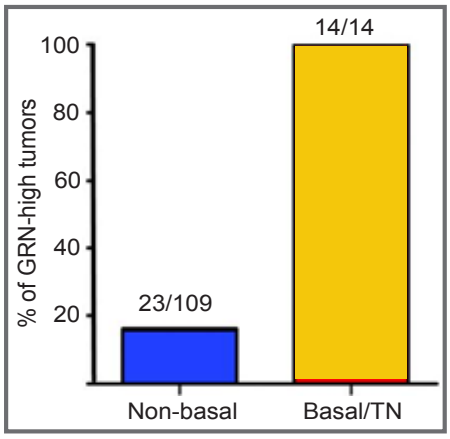
In Atlas Antibodies´ product catalog, there are two polyclonal Anti-GRN antibodies; HPA008763 and HPA028747.



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 glanduclar cells and vesicle positivity in U-251 MG cells.



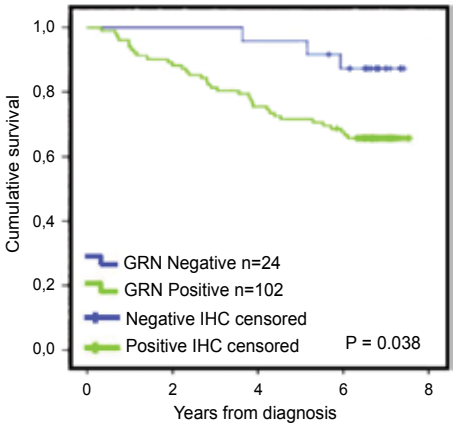


Figure 1
GRN expression was shown to correlate with aggressive tumor subtypes and reduced survival of breast cancer patients using antibody HPA028747. The diagram to the left shows percentage of tumors in each category (Triple-Negative [TN]/basal or nonbasal) that show high GRN positivity and the Kaplan-Meier analysis to the right shows correlation between GRN-positive (green) or GRN-negative (blue) expression and survival.

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.

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.

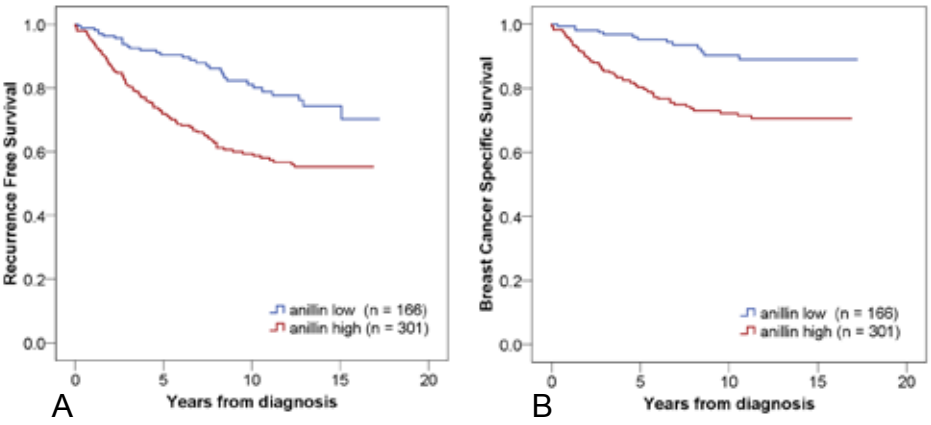
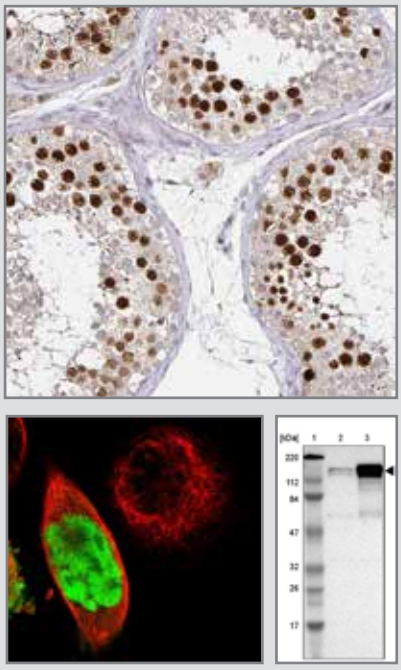


Figure 1
Kaplan-Meier (survival) analysis of recurrence free- (A) and breast cancer specific survival (B) according to aniliin expression for breast cancer patients. Patients were split into two groups based on high and low anillin expression.

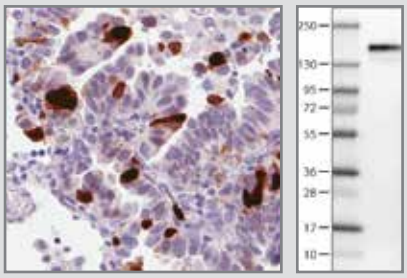
1. O´Leary PC *et al.* Systematic antibody generation and validation via tissue microarray technology leading to identification of a novel protein prognostic panel in breast cancer. *BMC Cancer.* 2013 Apr 2;13:175.

Anillin antibodies

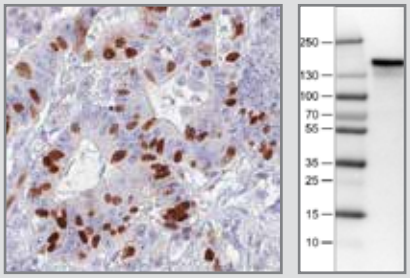
There are three Anti-ANLN antibodies in Atlas Antibodies product catalog; the mouse monoclonal antibodies AMAb90660 and AMAb90662 and the rabbit polyclonal HPA005680.



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.

Monoclonal Antibody Development Program

Research remains at the heart of Atlas Antibodies. We welcome customers to contact us for possible collaborations on both existing and future product offerings. One of our collaboration programs aims at developing monoclonal antibodies in collaboration with our customers.

Atlas Antibodies encourage you to participate in our Monoclonal Antibody Development Program for human targets. If you are looking for monoclonal antibodies currently not available in our catalog, and if you are interested in developing the antibody together with us, please send in your request to us.

Upon agreement to proceed with a collaboration, Atlas Antibodies will develop and produce the monoclonal antibody using our standardized procedures. Within this procedure we always epitope map all our clones and this will give you the possible option to obtain multiple clones with unique binding specificity. The selection of the optimal clones will be done in collaboration with you. Antibodies can either be sent to you for additional characterization in your laboratory or Atlas Antibodies can make the characterization at our facilities with our expert input and/or material. If the project results in a commercialized product it will be added to Atlas Antibodies Monoclonal product portfolio and available to you for a special discount price. All our final products will be stained and annotated by the Human Protein Atlas (HPA) project and these results will be available on the HPA web portal.

Benefits of the program

Atlas Antibodies take the full development cost while you get a discounted antibody with proven functionality in your experimental set-up.

For more information and/or requests for participating in the program, you are welcome to contact us at bd@atlasantibodies.com.

We are looking forward to hearing from you.

Collaboration project for SOX11

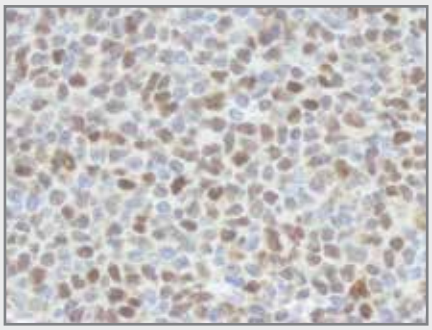
The mouse monoclonal Anti-SOX11 antibodies AMAb90501 and AMAb90502 were developed in collaboration with Dr Antonio Martinez (Laboratory of Pathology, Hospital Clínic, University of Barcelona, Spain).

Dr. Martinez is involved in the study of aggressive lymphomas, mechanisms of transformation, progression and prognostic factors. He has collaborated in the description of transcription factors involved in B-cell development and lymphomagenesis with special emphasis in those related in late B-cell differentiation pathways such as IRF4, IRF8, XBP1 and SOX11. His lab has long expertise in the characterization of antibodies for clinical use in hematopathology.

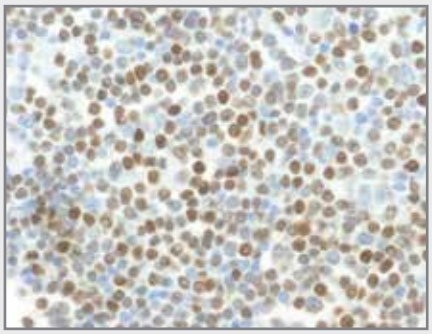
Soldini D *et al.* Assessment of SOX11 Expression in Routine Lymphoma Tissue Sections: Characterization of New Monoclonal Antibodies for Diagnosis of Mantle Cell Lymphoma. *Am J Surg Pathol.* 2013 Oct 18.

SOX11

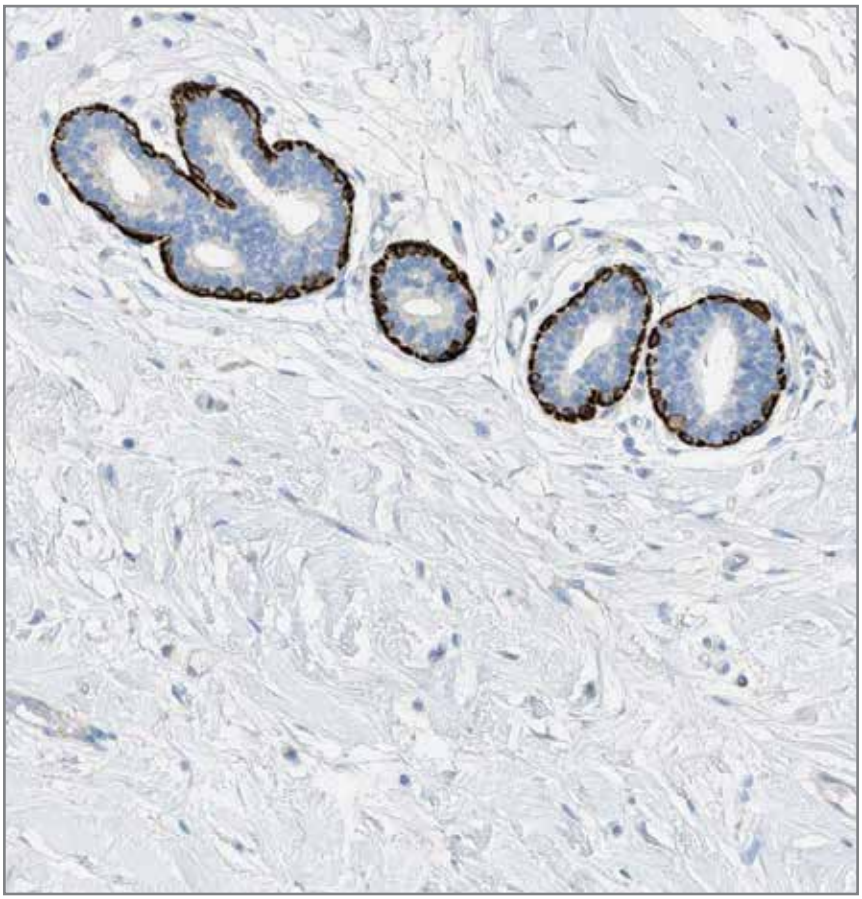
This gene encodes a member of the group C SOX (SRY-related HMG-box) transcription factor family involved in the regulation of embryonic development and in the determination of the cell fate. The encoded protein may act as a transcriptional regulator after forming a protein complex with other proteins. The protein may function in the developing nervous system and play a role in tumorigenesis and adult neurogenesis. Diseases associated with SOX11 include mantle cell lymphoma (MCL), lymphoblastic lymphoma, Burkitt lymphoma and malignant glioma. The diagnosis of mantle cell lymphoma can be difficult, especially in Cyclin D1 negative cases and the transcription factor SOX11 may serve as an important diagnostic marker. For this purpose, there is a need of a reliable Anti-SOX11 antibody in the clinical setting.



Tonsil involved by a Classical Mantle cell lymphoma, cyclin D1 negative in a 50 yo male. SOX11 staining (AMAb90501, clone CL0142; Atlas Antibodies).



Lymph node involvement by Classical Mantle cell lymphoma positive for Cyclin D1 in a 64 yo male. SOX11 is expressed in virtually all tumor cells. (AMAb90502, clone CL0143; Atlas Antibodies).



Anti-MYH11 (HPA015310) in human breast tissue.

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