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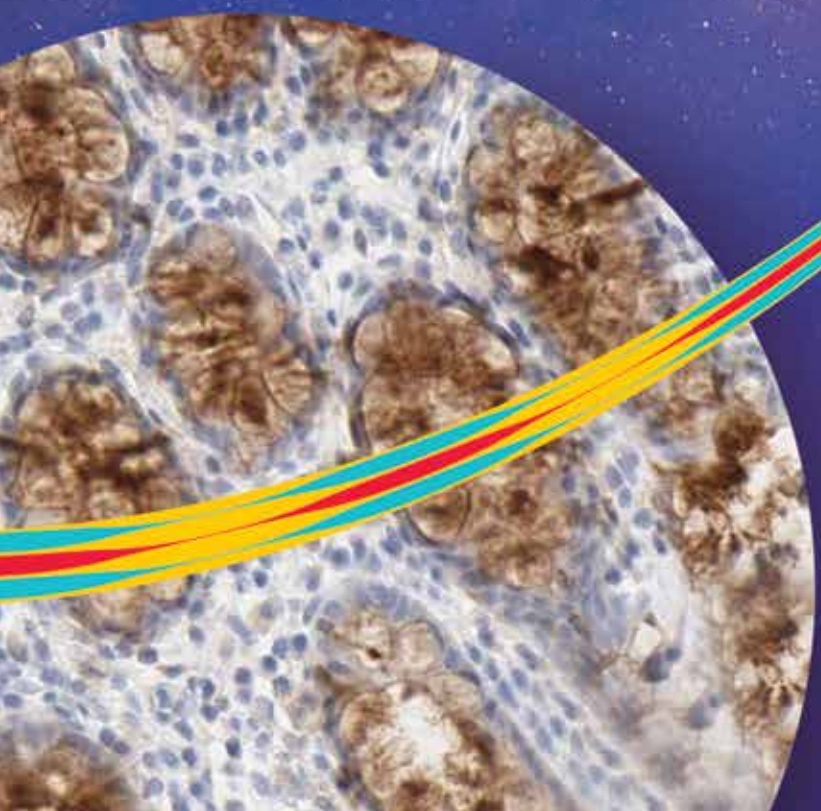
Prestige Antibodies® in Colorectal Cancer Research

ATLAS ANTIBODIES



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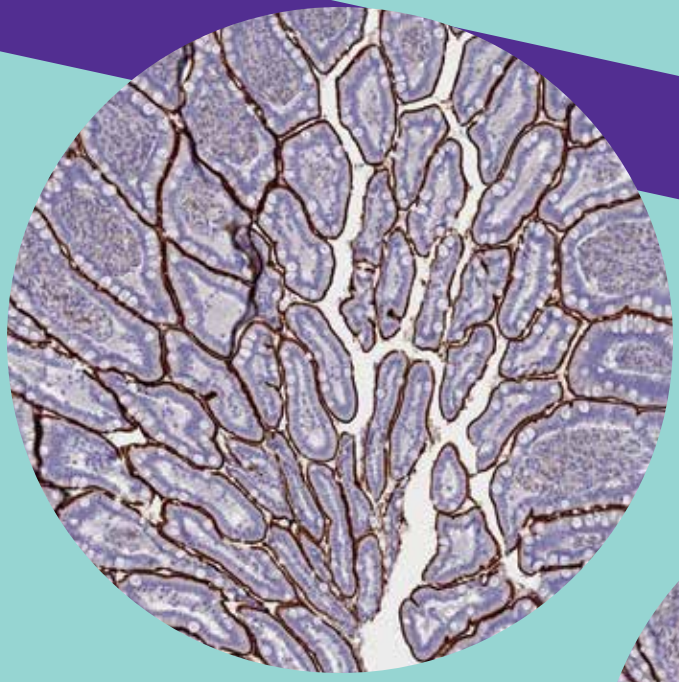
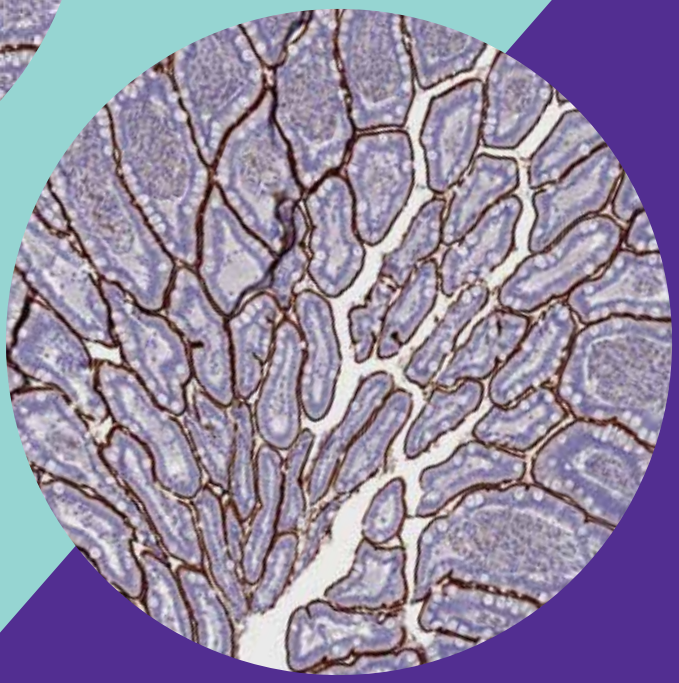
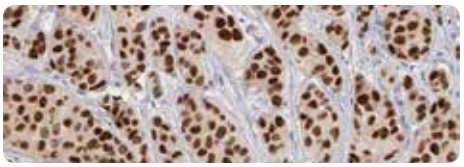
MERCK

Prestige Antibodies® in Colorectal Cancer Research

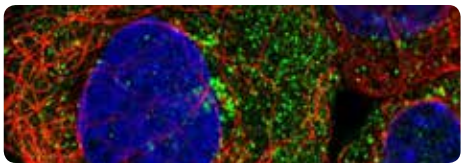




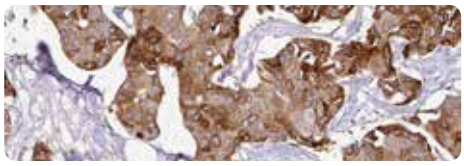
The Human Protein Atlas



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[1,2]. 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 Uhlén, and funded by the Knut and Alice Wallenberg foundation. It is a unique world leading effort performing systematic exploration ofthe 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 expressiondata 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 Normal GI tract Tissue and Colorectal Cancer Tissue Samples

IHC images from normal gastrointestinal tract samples from three different individuals are available for each antibody in the normal Tissue Atlas. The gastrointestinal tract tissues include colon, small intestine, duodenum, rectum, stomach, esophagus, salivary gland and oral mucosa.

In addition, for each antibody, colorectal tumor samples from up to 12 patients in duplicates are presented in the Cancer Atlas.

References:
1.Uhlén M *et al*. (2015) Tissue-based map of the human proteome. *Science* 347(6220):1260419.

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

Prestige Polyclonals

The uniqueness and specificity of Prestige Polyclonals 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 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 21,000 Prestige Polyclonals.

The antibodies developed and characterized within the Human Protein Atlas project are supplied by Merck under the brand name Prestige Polyclonals. The product numbers of Prestige Polyclonals start with “HPA”.

Prestige Monoclonals

We also provide a selected number of mouse monoclonal antibodies, under the brand name Prestige Monoclonals. The Prestige Monoclonal catalog is regularly expanding with hundreds of 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 Prestige 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 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” change to “In-vitro methods are used for the production scale up phase

Antibody Characterization
The characterization of Prestige Monoclonals starts with a thorough selection of the most relevant and clinically significant tissues to use for IHC characterization. In addition to positive stained tissues, 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.

Prestige Monoclonals are developed based on the knowledge from the Human Protein Atlas with careful antigen design and extended validation of antibody performance. With precise epitope information following all monoclonals, these precise, accurate and targeted antibodies are denoted Prestige Monoclonals.The product numbers of Prestige Monoclonals start with ”AMAb”.

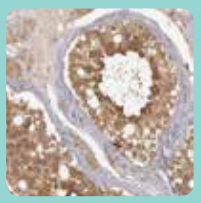
Antibodies Used In Colorectal Cancer Research

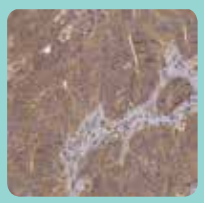
In this section, antibodies are selected either on a reference/article-basis or on colon cancer relevance for the corresponding target protein.

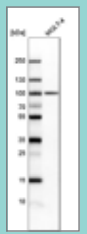
Target Protein	Product Name	Product Number	Validated Applications
ABCB1/CD243	**Anti-ABCB1**	HPA002199[1-2]	IHC,ICC-IF
ALCAM/CD166 antigen	**Anti-ALCAM**	HPA010926[3-5]	IHC
AOC3/HPAO	**ANTI-AOC3**	HPA000980[6-8]	IHC,WB
APC	**Anti-APC**	HPA013349	IHC
AXL	**Anti-AXL**	HPA037422[9-10]	IHC,WB
B-Raf	**Anti-BRAF**	HPA001328[11-13]	IHC
B-Raf	**Anti-BRAF**	HPA071048	ICC-IF,WB
B-Raf	**Anti-BRAF**	AMAb91257	IHC,WB
B-Raf	**Anti-BRAF**	AMAb91258	IHC,WB
BCL9	**Anti-BCL9**	HPA020274	IHC,ICC-IF
Bloom syn-drome prot	**Anti-BLM**	HPA005689[14-15]	IHC,ICC-IF
Cadherin-17	**Anti-CDH17**	HPA023616[16]	IHC,WB,ICC-IF
Cadherin-17	**Anti-CDH17**	HPA026556	IHC,WB,ICC-IF
Caldesmon	**Anti-CALD1**	HPA008066[17-20]	IHC,WB,ICC-IF
Caspase-3	**Anti-CASP3**	HPA002643[21-22]	IHC,WB,ICC-IF
Catenin beta-1	**Anti-CTNNB1**	HPA029159	IHC,WB,ICC-IF
Catenin beta-1	**Anti-CTNNB1**	HPA029160	IHC,ICC-IF
Catenin beta-1	**Anti-CTNNB1**	AMAb91209	IHC,WB
Catenin beta-1	**Anti-CTNNB1**	AMAb91210	IHC,WB
CDX-2	**Anti-CDX2**	HPA045669	ICC-IF
CDX-2	**Anti-CDX2**	HPA049580	ICC-IF

Target Protein	Product Name	Product Number	Validated Applications
CEACAM1/3/5/6	**Anti-CEACAM1**	HPA011041	IHC,WB
Chromogranin-A	**Anti-CHGA**	HPA017369[23-25]	IHC,WB,ICC-IF
Cytokeratin 18	**Anti-KRT18**	HPA001605	IHC,WB,ICC-IF
Cytokeratin 19	**Anti-KRT19**	HPA002465	IHC,WB,ICC-IF
Cytokeratin 20	**Anti-KRT20**	HPA024309	IHC,WB
Cytokeratin 20	**Anti-KRT20**	HPA024684	IHC,WB,ICC-IF
Cytokeratin 20	**Anti-KRT20**	HPA027236	IHC,WB
Cytokeratin 8	**Anti-KRT8**	HPA049866	IHC,WB,ICC-IF
DACH1	**Anti-DACH1**	HPA012672[26-28]	IHC,ICC-IF
DCC	**Anti-DCC**	HPA055376	ICC-IF
DCC	**Anti-DCC**	HPA069552	IHC
DTL	**Anti-DTL**	HPA028016[29]	IHC,WB
EGFR	**Anti-EGFR**	HPA001200[30]	IHC
EGFR	**Anti-EGFR**	HPA018530[31-32]	IHC,ICC-IF
EGFR	**Anti-EGFR**	AMAb90816	IHC,WB
FCGRT	**Anti-FCGRT**	HPA012122[33-35]	IHC,WB
Fibronectin	**Anti-FN1**	HPA027066[36]	IHC,WB
FOXRED1	**Anti-FOXRED1**	HPA046192[37]	IHC
GDF15	**Anti-GDF15**	HPA011191[38-42]	IHC,WB,ICC-IF
GPA33	**Anti-GPA33**	HPA018858[43-44]	IHC
GRHL2	**Anti-GRHL2**	HPA004820[45-49]	IHC,WB

Anti-BRAF (HPA001328)

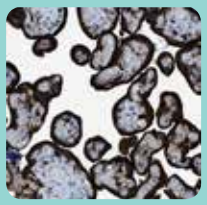


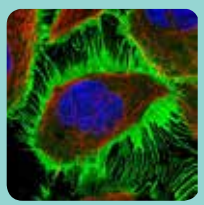




The Anti-BRAF antibody (HPA001328) shows cytoplasmic positivity in cells in seminiferous ducts in normal human testis as well as in tumor cells in colorectal cancer using immunohistochemistry. The HPA001328 antibody detects BRAF in human cell line MOLT-4 lysate using Western Blot analysis. Western blot analysis in human cell line MOLT-4.

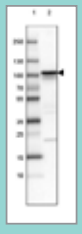
Anti-EGFR (HPA018530)





The Anti-EGFR antibody (HPA018530) shows strong cytoplasmic positivity in trophoblastic cells in human placenta tissue using IHC. By ICC-IF, the antibody shows strong positivity in plasma membrane in human cell line A-431 and in Western blot analysis, EGFR is detected in human cell line A-549 lysate.

Anti-CTNNB1 (AMAb91210)



IHC staining using the Anti-CTNNB1 (AMAb91210) antibody shows strong membranous immunoreactivity in epithelial cells in normal small intestine and in tumor cells in colorectal cancer tissues. By WB analysis, Catenin beta-1 is detected in human cell line A-431.

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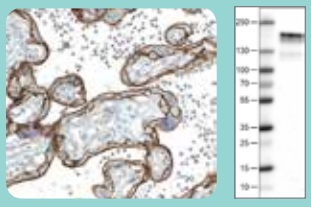
Anti-EGFR (AMAb90816)



The Anti-EGFR (AMAb90816) shows strong membranous positivity in trophoblasts in human placenta tissue using IHC and by Western Blot analysis, EGFR is detected in human A-431 cell line lysate.

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Antibodies Used In Colorectal Cancer Research (continued)

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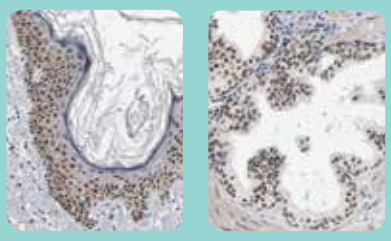
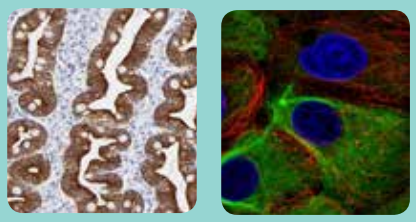
Anti-GRHL2 (HPA004820)



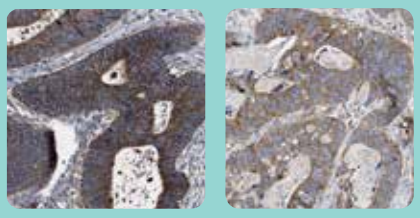
The Anti-GRHL2 antibody (HPA004820) shows strong nuclear positivity in glandular cells in human prostate tissue as well as in squamous epithelial cells in human skin tissue using IHC.

Anti-KRT19 (HPA002465)



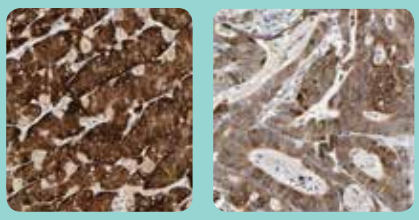
The Anti-KRT19 antibody (HPA002465) shows strong cytoplasmic and membranous positivity in glandular cells in human duodenum tissue using IHC. ICC-IF staining of human cell line MCF7 shows localization to intermediate filaments.

Anti-MACC1 (HPA020103)



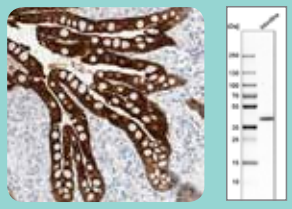
The Anti-KRT20 antibody (HPA024309) shows strong cytoplasmic and membranous positivity in glandular cells in colon tissue using IHC. Cytokeratin 20 ist detected using Western blot analysis in small intestine tissue lysate.

Anti-MUC1 (HPA004179)



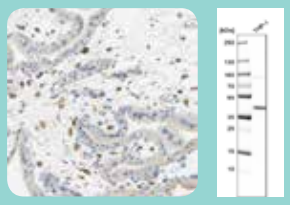
The Anti-MUC1 antibody (HPA004179) shows cytoplasmic and membranous positivity in glandular cells in normal stomach and in tumor cells in colorectal cancer.

Anti-KRT20 (HPA024309)



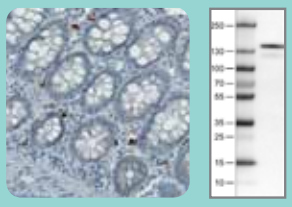
The Anti-KRT20 antibody (HPA024309) shows strong cytoplasmic and membranous positivity in glandular cells in colon tissue using IHC. Cytokeratin 20 ist detected using Western blot analysis in small intestine tissue lysate.

Anti-FCGRT (HPA012122)



By IHC, the Anti-FCGRT antibody (HPA012122) shows cytoplasmic positivity in Hofbauer cells in human placenta tissue. In Western blot analysis , FCGRT is detected in human cell line THP1 lysate.

Anti-KIT (AMAb90901)



The Anti-KIT antibody (AMAb90901) shows strong immunoreactivity in a subset of lymphoid cells (macrophages) in colon tissue. In Western blot analysis , KIT is detected in human cell line RT-4 lysate.

Target Protein	Product Name	Product Number	Validated Applications
Guanylin	**Anti-GUCA2A**	HPA018215[50-52]	IHC,WB
HMGCR	**Anti-HMGCR**	HPA008338[53-55]	IHC
HRH4	**Anti-HRH4**	HPA035009[56]	IHC
HTRB	**Anti-HTRB**	HPA012867[57-59]	IHC,ICC-IF
IDH1	**Anti-IDH1**	HPA035248[60]	IHC,WB
IGFBP7/IBP-7	**Anti-IGFBP7**	HPA002196[61-63]	IHC,WB
Integrin alpha-6	**Anti-ITGA6**	HPA012696[64-65]	IHC,WB
IRF2BP1	**Anti-IRF2BP1**	HPA042164[66]	IHC,WB
KIT	**Anti-KIT**	AMAb90901	IHC,WB
KIT	**Anti-KIT**	AMAb90904	IHC,WB
KIT	**Anti-KIT**	HPA004471	IHC
KIT	**Anti-KIT**	HPA073252	ICC-IF
KRAS/HRAS/NRAS	**Anti-KRAS**	HPA049830	IHC
LAMB2/S-LAM beta	**Anti-LAMB2**	HPA001895[67]	IHC,WB
LCN2/NGAL/p25	**Anti-LCN2**	HPA002695[68-70]	IHC,WB
LGR5	**Anti-LGR5**	HPA012530[71-74]	IHC,WB

Target Protein	Product Name	Product Number	Validated Applications
LMAN1/ER-GIC-53	**Anti-LMAN1**	HPA002320[75]	IHC,WB
LPAR2	**Anti-LPAR2**	HPA019616[76-78]	IHC,WB
LPAR3	**Anti-LPAR3**	HPA013421[79]	IHC,WB,ICC-IF
MACC1	**Anti-MACC1**	HPA020103[80-81]	IHC,WB
MAP1B	**Anti-MAP1B**	HPA022275[82-83]	IHC,ICC-IF
MCAM/MUC18	**Anti-MCAM**	HPA008848[84]	IHC
MGAT5/GNT-V	**Anti-MGAT5**	HPA010919	IHC,WB
MLH1/COCA2	**Anti-MLH1**	HPA052707	IHC,WB,ICC-IF
MLH1/COCA2	**Anti-MLH1**	HPA060714	ICC-IF
MSH6/GTBP	**Anti-MSH6**	HPA028376	IHC,WB,ICC-IF
MSH6/GTBP	**Anti-MSH6**	HPA028446	IHC
MUC3/MUC3A	**Anti-MUC3A**	HPA010871	IHC
Mucin-1	**Anti-MUC1**	HPA004179	IHC,WB
Mucin-1	**Anti-MUC1**	HPA007235	IHC
Mucin-1	**Anti-MUC1**	HPA008855[85]	IHC,ICC-IF
NDRG1	**Anti-NDRG1**	HPA006881[86-89]	IHC,WB,ICC-IF

Antibodies Used In Colorectal Cancer Research (continued)

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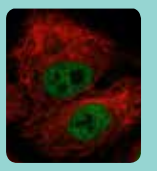
Target Protein	Product Name	Product Number	Validated Applications
Nucleophosmin	**Anti-NPM1**	HPA011384[90-91]	IHC,WB,ICC-IF
P53	**Anti-P53 Antibody**	AMAb90956[92]	IHC,WB,ICC-IF
PARP6	**Anti-PARP6**	HPA026991[93-94]	IHC,ICC-IF
Periostin	**Anti-POSTN**	HPA012306[95-96]	IHC,WB
PIK3CA	**Anti-PIK3CA**	HPA009985[97-99]	IHC,ICC-IF
Plexin-B1	**Anti-PLXNB1**	HPA040586[100]	IHC
PMS2/PMSL2	**Anti-PMS2**	HPA070310	ICC-IF
PMS2/PMSL2	**Anti-PMS2**	HPA066490	ICC-IF
Podocalyxin	**Anti-PODXL**	HPA002110[101-105]	IHC,WB,ICC-IF
PTP4A1/2/3	**Anti-PTP4A1**	HPA003281	IHC,WB
RBM3	**Anti-RBM3**	AMAb90655[106-110]	IHC,WB,ICC-IF
RBM3	**Anti-RBM3**	HPA003624[111-113]	IHC,WB,ICC-IF
RECQL5	**Anti-RECQL5**	HPA029971[114-116]	IHC,WB,ICC-IF
RET	**Anti-RET**	HPA008356[117-118]	IHC,ICC-IF
RIBC2	**Anti-RIBC2**	HPA003210[119]	IHC
ROBO2	**Anti-ROBO2**	HPA013371[120]	IHC,WB,ICC-IF
SATB2	**Anti-SATB2**	HPA029543[121]	IHC,ICC-IF
SATB2	**Anti-SATB2**	AMAb90679	IHC,WB
Semaphorin-4D	**Anti-SEMA4D**	HPA015662	IHC,WB
Serpin A1	**Anti-SERPINA1**	HPA000927	IHC,WB,ICC-IF
SIX1	**Anti-SIX1**	HPA001893	IHC,WB,ICC-IF
SORD	**Anti-SORD**	HPA040260	IHC,WB,ICC-IF
SOX9	**Anti-SOX9**	HPA001758	IHC,WB,ICC-IF

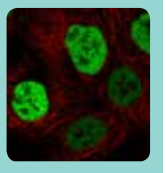
Target Protein	Product Name	Product Number	Validated Applications
SOX21	**Anti-SOX21**	AMAb91309	IHC,WB
SOX21	**Anti-SOX21**	AMAb91311	IHC,WB
SRC	**Anti-SRC**	HPA030875	IHC,WB,ICC-IF
SRSF5	**Anti-SRSF5**	HPA043484[122]	IHC,WB,ICC-IF
SRSF6	**Anti-SRSF6**	HPA029005[123]	IHC,WB
SRSF7	**Anti-SRSF7**	HPA043850[124]	IHC,WB,ICC-IF
STK4/MST-1	**Anti-STK4**	HPA015270[125]	IHC,WB,ICC-IF
SUSD2	**Anti-SUSD2**	HPA004117[126-127]	IHC,ICC-IF
TAK1/TR4/NR2C2	**Anti-NR2C2**	HPA006313	IHC,WB,ICC-IF
TET1	**Anti-TET1**	HPA019032[128-129]	IHC,ICC-IF
TFAP4	**Anti-TFAP4**	HPA001912[130]	IHC,WB,ICC-IF
TGFB1	**Anti-TGFB1**	HPA008612[131-133]	IHC,WB
TIMP1/EPA	**Anti-TIMP1**	HPA053417	IHC
TJP1	**Anti-TJP1**	HPA001636[134-135]	IHC,WB,ICC-IF
TNIK	**Anti-TNIK**	HPA012128[136-137]	IHC,ICC-IF
TRAF6	**Anti-TRAF6**	HPA019805	IHC,WB,ICC-IF
TRAF6	**Anti-TRAF6**	HPA020599	IHC,WB
Transgelin	**Anti-TAGLN**	HPA019467[138]	IHC,WB,ICC-IF
Willin/FRMD6	**Anti-FRMD6**	HPA001297[139]	IHC,WB,ICC-IF
YWHAB/KCIP-1	**Anti-YWHAB**	HPA011212[140]	IHC,WB,ICC-IF
ZEB1/TCF-8	**Anti-ZEB1**	HPA027524[141-145]	IHC,WB,ICC-IF
ZEB1/TCF-8	**Anti-ZEB1**	AMAb90510	IHC,WB,ICC-IF
Zyxin	**Anti-ZYX**	HPA004835[146]	IHC,WB,ICC-IF

Anti-ZEB1 (AMAb90510)

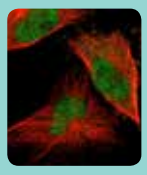
Shows strong nuclear positivity in the stromal, but not glandular cells in endometrium tissue using IHC. ICC-IF shows nuclear staining in the human A-549 cell line. The antibody signal is downregulated using ZEB1-specific siRNA probes in extracts from RH-30 cells, shown by WB analysis.

ANTI-P53 (AMAb90956)

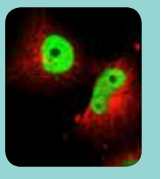
Shows strong nuclear immunoreactivity in tumor cells in human colorectal cancer using IHC. ICC-IF staining in A431 cell line shows cell cycle dependent nuclear (without nucleoli) staining. The antibody signal is downregulated using p53-specific siRNA probes in extracts from U-251 cells, shown by WB analysis.

ANTI-SIX1 (HPA001893)

Shows strong nuclear positivity in striated muscle fibers in human skeletal muscle using IHC. ICC-IF staining of human cell line U-251 MG shows positivity in nucleus but excluded from the nucleoli. Western blot analysis detects SIX1 in human cell line RH-30.

ANTI-SOX9 (HPA001758)

Shows moderate to strong nuclear positivity in tumor cells in human colorectal cancer using IHC. ICC-IF staining of human cell line U-251 MG shows positivity in nucleus but excluded from the nucleoli. Western blot analysis detects SOX9 in human cell line HepG2.

Antibodies against gene products in Oncotype and Coloprint tests

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.

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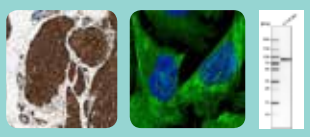
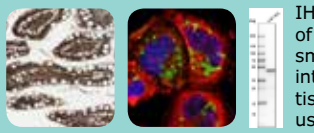
Anti-CALD1 (HPA008066)



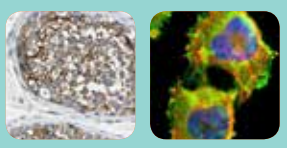
IHC staining of human smooth muscle tissue using the Anti-CALD1 antibody (HPA008066) shows cytoplasmic positivity in smooth muscle cells. Using ICC-IF in U2-OS cells, the antibody stains actin filament and plasma membrane. CALD1 is detected in cell line U-138 MG cell line.

Anti-PLIN3 (HPA006427)



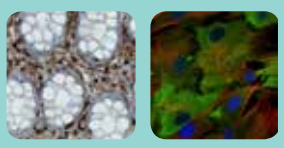
IHC staining of human small intestine tissue using the Anti-PLIN3 antibody (HPA006427) shows positivity in glandular cells. ICC-IF in A-431 cell line shows positivity in lipid droplets. PLIN3 is detedted in cell line U-87 MG lysate using WB analysis.

Anti-AKAP12 (HPA006344)



IHC staining of human testis tissue using the Anti-AKAP12 antibody (HPA006344) shows cytoplasmic and membranous positivity in seminiferous ducts. ICC-IF staining of human cell line U-251 MG shows localization to plasma membrane and cytosol.

Anti-S100A4 (AMAb90598)



IHC staining of human rectum tissue using the Anti-S100A4 antibody (AMAb90598) shows strong immunoreactivity in a subset of lymphoid cells. In ICC-IF, in BJ cells, plasma membrane is stained.

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J Cell Biochem 2012 May; 113(5):1569-1580.

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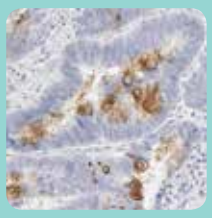
Target Protein	Product Name	Product Number	Validated Applications
AKAP12	**Anti-AKAP12**	HPA006344[1]	IHC,ICC-IF
AKAP12	**Anti-AKAP12**	HPA056230	IHC,ICC-IF
AKT3	**Anti-AKT3**	HPA026441[2-4]	IHC,WB
Caldesmon	**Anti-CALD1**	HPA008066[5-8]	IHC,WB,ICC-IF
Caldesmon	**Anti-CALD1**	HPA017330[9-11]	IHC,WB,ICC-IF
ANTXR1	**Anti-ANTXR1**	HPA052046	IHC
Biglycan	**Anti-BGN**	HPA003157[12-13]	IHC,WB,ICC-IF
Collagen alpha-1	**Anti-COL1A1**	HPA008405	IHC
Collagen alpha-1	**Anti-COL1A1**	HPA011795	IHC,ICC-IF
SPARC	**Anti-SPARC**	HPA002989[14]	IHC,WB
SPARC	**Anti-SPARC**	HPA003020[15]	IHC,WB
CTHRC1/NMTC1	**Anti-CTHRC1**	HPA059806	IHC,WB
FAP	**Anti-FAP**	HPA059739	IHC
Inhibin beta A chain	**Anti-INHBA**	HPA020031[16-18]	IHC
LOXL2	**Anti-LOXL2**	HPA036257	ICC-IF
LOXL2	**Anti-LOXL2**	HPA056542	ICC-IF
TGFB3	**Anti-TGFB3**	HPA063582	ICC-IF
PDGFC	**Anti-PDGFC**	HPA009134	IHC,ICC-IF
IGFBP7	**Anti-IGFBP7**	HPA002196[19-21]	IHC,WB
SFRP4	**Anti-SFRP4**	HPA009712	IHC,WB
SFRP4	**Anti-SFRP4**	HPA050585	IHC,WB
DLC1	**Anti-DLC1**	HPA017753[22]	IHC,WB,ICC-IF
EGR1	**Anti-EGR1**	HPA029938	ICC-IF
EGR1	**Anti-EGR1**	HPA029937	ICC-IF
GADD45B	**Anti-GADD45B**	HPA029816[23]	IHC,ICC-IF
SERPINE1/PAI1	**Anti-SERPINE1**	HPA050039[24]	IHC,ICC-IF
SPP1/OPN	**Anti-SPP1**	HPA027541[25]	IHC,WB
S100A4	**Anti-S100A4**	HPA007973[26-27]	IHC,WB
S100A4	**Anti-S100A4**	AMAb90596	IHC,WB,ICC-IF
S100A4	**Anti-S100A4**	AMAb90598	IHC,WB,ICC-IF
S100A4	**Anti-S100A4**	AMAb90599	IHC,WB,ICC-IF
HSPA1A	**Anti-HSPA1A**	HPA052504	IHC,WB
TGFBI	**Anti-TGFBI**	HPA008612[28-30]	IHC,WB
TGFBI	**Anti-TGFBI**	HPA017019	IHC,WB
GRB10	**Anti-GRB10**	HPA027502	IHC
LAMC2	**Anti-LAMC2**	HPA024638	IHC
LAMC2	**Anti-LAMC2**	AMAb91098	IHC,WB
CDKN2A/P14ARF	**Anti-CDKN2A**	HPA047838	ICC-IF
CDC20	**Anti-CDC20**	HPA055288	IHC,WB
CDC20	**Anti-CDC20**	HPA045842	ICC-IF
Ki-67/MKI67	**Anti-MKI67**	AMAb90870	IHC

Target Protein	Product Name	Product Number	Validated Applications
Ki-67/MKI67	**Anti-MKI67**	HPA000451[31-32]	IHC,ICC-IF
Ki-67/MKI67	**Anti-MKI67**	HPA001164[33]	IHC,ICC-IF
MCM2	**Anti-MCM2**	HPA031495	IHC,WB,ICC-IF
MCM2	**Anti-MCM2**	HPA031496	IHC,WB,ICC-IF
RRM1	**Anti-RRM1**	HPA057265	IHC,ICC-IF
RRM1	**Anti-RRM1**	HPA064297	IHC
RRM2	**Anti-RRM2**	HPA056994	IHC,WB,ICC-IF
SKP2	**Anti-SKP2**	HPA051196	WB,ICC-IF
SKP2	**Anti-SKP2**	HPA054633	IHC,WB
MYC/CMYC	**Anti-MYC**	HPA055893	IHC,ICC-IF
MYC/CMYC	**Anti-MYC**	HPA066556	ICC-IF
CSEL1/CSE1L	**Anti-CSE1L**	HPA038059	IHC,WB,ICC-IF
CSEL1/CSE1L	**Anti-CSE1L**	HPA038060	IHC,ICC-IF
MYBL2	**Anti-MYBL2**	HPA030530	IHC,WB
MYBL2	**Anti-MYBL2**	HPA055416	ICC-IF
NME1/GAAD	**Anti-NME1**	HPA008467[34]	IHC,WB,ICC-IF
NME1/GAAD	**Anti-NME1**	HPA041113	IHC,WB
UMPS/OPRT	**Anti-UMPS**	HPA036178	IHC,WB,ICC-IF
UMPS/OPRT	**Anti-UMPS**	HPA036179	IHC
HNRPD	**Anti-HNRNPD**	HPA004911	IHC,WB,ICC-IF
MCTP1	**Anti-MCTP1**	HPA019018	IHC,WB,ICC-IF
LAMA3	**Anti-LAMA3**	HPA009309	IHC
LAMA3	**Anti-LAMA3**	AMAb91123	IHC,WB
CTSC/Cathepsin C	**Anti-CTSC**	HPA066610	WB,ICC-IF
PYROXD1	**Anti-PYROXD1**	HPA038319	IHC,WB
PYROXD1	**Anti-PYROXD1**	HPA038320	IHC,WB,ICC-IF
EDEM1	**Anti-EDEM1**	HPA029565	IHC,ICC-IF
IL2RB/CD122	**Anti-IL2RB**	HPA062657	IHC,WB
ZNF697	**Anti-ZNF697**	HPA049933	IHC,ICC-IF
SLC6A11/GAT-3	**Anti-SLC6A11**	HPA037981	IHC,WB
IL2RA/CD25	**Anti-IL2RA**	HPA054622	IHC
CYFIP2	**Anti-CYFIP1**	HPA068106	IHC,WB
PIM3	**Anti-PIM3**	HPA068758	ICC-IF
LIF	**Anti-LIF**	HPA018844	IHC,ICC-IF
Perilipin-3/PLIN3	**Anti-PLIN3**	HPA006427[35]	IHC,WB,ICC-IF
Perilipin-3/PLIN3	**Anti-PLIN3**	HPA066538	IHC,WB,ICC-IF
HSD3B1	**Anti-HSD3B1**	HPA043261	IHC
HSD3B1	**Anti-HSD3B1**	HPA043264	IHC
HSD3B1	**Anti-HSD3B1**	HPA044028	IHC
ZBED4	**Anti-ZBED4**	HPA045341	IHC,ICC-IF
PPARA	**Anti-PPARA**	HPA067049	WB,ICC-IF
THNSL2	**Anti-THNSL2**	HPA035395	IHC

Antibodies against gene products elevated in colon identified in the Human Protein Atlas

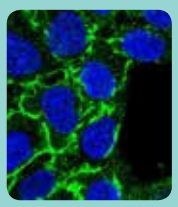
The genes included in this section show at least 5-fold higher mRNA levels in colon tissue compared to all other human tissues. Antibodies against these gene products are presented.

Anti-FCGBP (HPA003564)



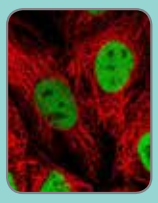
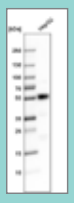

The Anti-FCGBP antibody (HPA003564) shows strong cytoplasmic positivity in glandular cells in human colorectal cancer and normal rectum tissue using IHC.

Anti-CDH17 (HPA023614)

The Anti-CDH17 antibody (HPA023614) shows membranous positivity in glandular cells in human duodenum tissue using IHC. In ICC-IF, CDH17 is localized to cell junctions in human cell line CACO-2.

Anti-HNF4A (HPA004712)

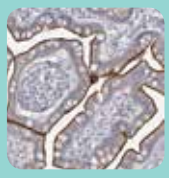
The Anti-HNF4A antibody (HPA004712) shows strong nuclear positivity in glandular cells in human small intestine using IHC. Using ICC-IF, HNF4A was localized to nucleoplasm in cell line CACO-2. HNF4A was detected in human cell line HepG2 using WB analysis.

Anti-PIGR (HPA012012)



The Anti-PIGR antibody (HPA012012) shows strong cytoplasmic and membranous positivity in glandular cells in human colon and in tumor cells in colorectal cancer tissue using IHC. PIGR is detected in colon tissue lysate using Western blot analysis.

Anti-SLC9A3 (HPA036669)

The Anti-SLC9A3 antibody (HPA036669) shows strong apical membrane positivity in glandular cells in human small intestine and in colorectal cancer tissues using immunohistochemistry.

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2. 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.

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16. 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.

17. 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.

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19. 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.

20. 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. Epub 2012 Mar 8.

Target Protein	Product Name	Product Number	Validated Applications
B3GNT6	**Anti-B3GNT6**	HPA039805	IHC
C10orf99	**Anti-C10orf99**	HPA050920	IHC
CA1	**Anti-CA1**	HPA006558	IHC
CA2	**Anti-CA2**	HPA001550[1]	IHC,WB
CD177	**Anti-CD177**	HPA041820	IHC
CD177	**Anti-CD177**	HPA046601	IHC
CDH17	**Anti-CDH17**	HPA023614	IHC,WB
CDH17	**Anti-CDH17**	HPA023616[2]	IHC,WB,ICC-IF
CDH17	**Anti-CDH17**	HPA026556	IHC,WB,ICC-IF
CDHR5	**Anti-CDHR5**	HPA009081	IHC
CDHR5	**Anti-CDHR5**	HPA009173	IHC,WB
CDX1	**Anti-CDX1**	HPA055196	IHC
CDX2	**Anti-CDX2**	HPA045669	ICC-IF
CDX2	**Anti-CDX2**	HPA049580	ICC-IF
CEACAM1/3/5/6	**Anti-CEA-CAM1**	HPA011041	IHC,WB
CEACAM5	**Anti-CEA-CAM5**	HPA019758	IHC,WB,ICC-IF
CEACAM7	**Anti-CEA-CAM7**	HPA069621	IHC
Claudin-3	**Anti-CLDN3**	HPA014361	IHC,ICC-IF
CLCA1	**Anti-CLCA1**	HPA052787	IHC
CLCA1	**Anti-CLCA1**	HPA059301	IHC
DHRS11	**Anti-DHRS11**	HPA041226	IHC,ICC-IF
DHRS11	**Anti-DHRS11**	HPA048236	IHC
DHRS11	**Anti-DHRS11**	HPA053623	IHC
ENTPD8	**Anti-ENTPD8**	HPA021509	IHC,ICC-IF
FABP1	**Anti-FABP1**	HPA028275	IHC,WB,ICC-IF
FCGBP	**Anti-FCGBP**	HPA003517[3]	IHC
FCGBP	**Anti-FCGBP**	HPA003564	IHC,ICC-IF
FUT3/5/6	**Anti-FUT3**	HPA046966	IHC
FXYD3	**Anti-FXYD3**	HPA010856[4]	IHC,ICC-IF
GAL3ST2	**Anti-GAL3ST2**	HPA071809	IHC
Galectin-4	**Anti-LGALS4**	HPA031184	IHC
Galectin-4	**Anti-LGALS4**	HPA031185	IHC
Galectin-4	**Anti-LGALS4**	HPA031186	IHC,WB
GPA33	**Anti-GPA33**	HPA018858	IHC
GUCA2A	**Anti-GUCA2A**	HPA018215[5-7]	IHC,WB
HNF4A	**Anti-HNF4A**	HPA004712[8-9]	IHC,WB,ICC-IF
HSD11B2	**Anti-HSD11B2**	HPA042186	IHC

Target Protein	Product Name	Product Number	Validated Applications
HSD11B2	**Anti-HSD11B2**	HPA056385	IHC,ICC-IF
INSL5	**Anti-INSL5**	HPA030100	IHC,WB
Keratin 20	**Anti-KRT20**	HPA024309	IHC,WB
Keratin 20	**Anti-KRT20**	HPA024684	IHC,WB,ICC-IF
Keratin 20	**Anti-KRT20**	HPA027236	IHC,WB
MEP1A	**Anti-MEP1A**	HPA029416	IHC
MISP	**Anti-MISP**	HPA049511	IHC,WB,ICC-IF
MISP	**Anti-MISP**	HPA062232	IHC,WB,ICC-IF
MS4A12	**Anti-MS4A12**	HPA057657	IHC
MUC13	**Anti-MUC13**	HPA045163	IHC,WB
NOXO1	**Anti-NOXO1**	HPA071540	IHC,WB
NXPE1	**Anti-NXPE1**	HPA049133	IHC,WB
NXPE2	**Anti-NXPE2**	HPA039744	IHC
NXPE2	**Anti-NXPE2**	HPA039876	IHC
PADI2	**Anti-PADI2**	HPA047735	IHC,WB
PHGR1	**Anti-PHGR1**	HPA068787	IHC,ICC-IF
PIGR	**Anti-PIGR**	HPA006154	IHC
PIGR	**Anti-PIGR**	HPA012012[10-13]	IHC,WB
PYY	**Anti-PYY**	HPA010973	IHC
REG4	**Anti-REG4**	HPA046555	IHC
SATB2	**Anti-SATB2**	HPA001042[14-17]	IHC
SATB2	**Anti-SATB2**	HPA029543[18]	IHC,ICC-IF
SATB2	**Anti-SATB2**	AMAb90679	IHC,ICC-IF
SLC22A18AS	**Anti-SLC22A18AS**	HPA068288	IHC,WB,ICC-IF
SLC26A2	**Anti-SLC26A2**	HPA058090	IHC,WB
SLC9A3	**Anti-SLC9A3**	HPA036493	IHC,ICC-IF
SLC9A3	**Anti-SLC9A3**	HPA036669	IHC,WB
SPINK4	**Anti-SPINK4**	HPA007286	IHC,ICC-IF
SULT1B1	**Anti-SULT1B1**	HPA002107	IHC,WB,ICC-IF
Tetraspanin 8	**Anti-TSPAN8**	HPA044337	IHC,ICC-IF
TFF3	**Anti-TFF3**	HPA035464	IHC,ICC-IF
TPH1	**Anti-TPH1**	HPA022483	IHC
UGT2B17	**Anti-UGT2B4**	HPA045108	IHC
VIL1	**Anti-VIL1**	HPA006884[19]	IHC,WB,ICC-IF
VIL1	**Anti-VIL1**	HPA006885[20]	IHC,WB
VIP	**Anti-VIP**	HPA017324	IHC
ZG16	**Anti-ZG16**	HPA052066	IHC,WB
ZG16	**Anti-ZG16**	HPA052512	IHC,WB

Antibodies identified in the Human Protein Atlas

In this section, antibodies are selected based on identified differential IHC staining patterns in colon and colorectal cancer samples.

1. Tsuneki M *et al.* A Hydrogel-Endothelial Cell implant Mimics Infantile Hemangioma: Modulation by Survivin and the Hippo pathway*. *Lab Invest* 2015 May 11; 95(7):765-780. Epub 2015 May 11.

2. Zhou J *et al.* DACH1, a Zona Glomerulosa Selective Gene in the Human Adrenal, Activates Transforming Growth Factor-β Signaling and Suppresses Aldosterone Secretion. *Hypertension* 2015 May; 65(5):1103-1110. Epub 2015 Apr 8.

3. 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.

4. 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.

5. Stadler C *et al.* Immunofluorescence and fluorescent-protein tagging show high correlation for protein localization in mammalian cells. *Nat Methods* 2013 Apr; 10(4):315-23. Epub 2013 Feb 24.

6. Kim D *et al.* SHMT2 drives glioma cell survival in ischaemia but imposes a dependence on glycine clearance. *Nature* April 08, 2015.

7. Perisic L *et al.* Profiling of atherosclerotic lesions by gene and tissue microarrays reveals PCSK6 as a novel protease in unstable carotid atherosclerosis. *Arterioscler Thromb Vasc Biol* 2013 Oct; 33(10):2432-43. Epub 2013 Aug 1.

8. Ko YH *et al.* Glutamine fuels a vicious cycle of autophagy in the tumor stroma and oxidative mitochondrial metabolism in epithelial cancer cells: Implications for preventing chemotherapy resistance. *Cancer Biol Ther* 2011 Dec 15; 12(12):1085-1097. Epub 2011 Dec 15.

9. Stadler C *et al.* Immunofluorescence and fluorescent-protein tagging show high correlation for protein localization in mammalian cells. *Nat Methods* 2013 Apr; 10(4):315-23. Epub 2013 Feb 24.

10. Brown LJ *et al.* Chronic Reduction of the Cytosolic or Mitochondrial NAD(P)-malic Enzyme Does Not Affect Insulin Secretion in a Rat Insulinoma Cell Line. *J Biol Chem* 2009 Dec 18; 284(51):35359-35367. Epub 2009 Oct 26.

11. Zoccarato F *et al.* Succinate is the controller of O2-/H2O2 release at mitochondrial complex I : negative modulation by malate, positive by cyanide. *J Bioenerg Biomembr* 2009 Aug; 41(4):387-93. Epub 2009 Oct 10.

Product Name	Product Number	Validated Applications
Anti-ACADSB	HPA041458	IHC,WB,ICC-IF
Anti-ACBD7	HPA043326	IHC,ICC-IF
Anti-ACSL5	HPA007162	IHC,WB,ICC-IF
Anti-ADIRF	HPA026810	IHC,ICC-IF
Anti-AGR3	HPA053942	IHC,ICC-IF
Anti-AJUBA	HPA006171[1]	IHC,WB,ICC-IF
Anti-ALG14	HPA031829	IHC,ICC-IF
Anti-AN-KRD34C	HPA045329	IHC,ICC-IF
Anti-AOAH	HPA021666	IHC,WB
Anti-AQP3	HPA014924	IHC,WB,ICC-IF
Anti-ATF6	HPA005935	IHC
Anti-AT-P6V1B2	HPA008147	IHC,WB,ICC-IF
Anti-AVPR2	HPA046678	IHC
Anti-B3GNT8	HPA043669	IHC
Anti-BCL9	HPA020274	IHC,ICC-IF
Anti-CAND2	HPA005777	IHC,ICC-IF
Anti-CCDC-144NL	HPA023457	IHC,WB,ICC-IF
Anti-CDH12	HPA029325	IHC
Anti-CDK6	HPA002637	IHC,WB,ICC-IF
Anti-CLDN18	HPA018446	IHC
Anti-COG7	HPA040758	IHC,WB,ICC-IF
Anti-CPE	HPA003545	IHC
Anti-CPE	HPA003819	IHC,WB
Anti-CXorf67	HPA006128	IHC,ICC-IF
Anti-DACH1	HPA012672[2-4]	IHC,ICC-IF
Anti-DEFB115	HPA053160	IHC
Anti-FAM3D	HPA013844	IHC
Anti-FBXW12	HPA037491	IHC
Anti-FKBP7	HPA008707[5]	IHC,WB,ICC-IF
Anti-GAA	HPA026970	IHC,WB
Anti-GAK	HPA027463	IHC,ICC-IF
Anti-GALNT6	HPA011762	IHC,WB
Anti-GLB1L3	HPA039916	IHC
Anti-GLDC	HPA002318[6]	IHC,WB
Anti-GLUL	HPA007316[7-8]	IHC,WB
Anti-HEPH	HPA005824	IHC,WB
Anti-HLA-E	HPA031454	IHC,ICC-IF
Anti-HMGCS2	HPA027423	IHC,WB
Anti-HMGCS2	HPA027442	IHC,WB,ICC-IF
Anti-HNF4G	HPA005438	IHC
Anti-HPS6	HPA040687	IHC,WB

Product Name	Product Number	Validated Applications
Anti-IFITM3	HPA004337[9]	IHC,WB
Anti-ITGBL1	HPA005676	IHC,WB
Anti-KLHL8	HPA017762	IHC,ICC-IF
Anti-MAGEB1	HPA002820	IHC
Anti-ME2	HPA008247	IHC,WB,ICC-IF
Anti-ME2	HPA008880[10-14]	IHC,WB
Anti-METTL7B	HPA038644	IHC,WB,ICC-IF
Anti-MRS2	HPA017642	IHC,WB
Anti-MYBB-P1A	HPA005466	IHC,WB,ICC-IF
Anti-NAA-LADL2	HPA012413	IHC
Anti-NCBP3	HPA008959[15]	IHC,ICC-IF
Anti-OR9K2	HPA015808	IHC
Anti-OSBPL3	HPA000691[16]	IHC,WB,ICC-IF
Anti-P2RX6	HPA028776	IHC,ICC-IF
Anti-PFKFB2	HPA049975	IHC,ICC-IF
Anti-PHTF2	HPA012312	IHC,ICC-IF
Anti-PITX1	HPA008743	IHC,ICC-IF
Anti-PKN3	HPA045390	IHC
Anti-POMK	HPA013321	IHC,WB,ICC-IF
Anti-PPP1R35	HPA051607	IHC
Anti-PYGB	HPA031067	IHC,WB,ICC-IF
Anti-RAD18	HPA008752	IHC,WB,ICC-IF
Anti-REEP4	HPA042683	IHC,WB
Anti-REG1A	HPA045549	IHC,WB
Anti-RIPPLY2	HPA047454	IHC
Anti-RPS13	HPA005985	IHC,ICC-IF
Anti-S100A4	HPA007973[17-18]	IHC,WB
Anti-SATB2	HPA001042[19-22]	IHC
Anti-SOCS7	HPA004475[23]	IHC,ICC-IF
Anti-SQLE	HPA018038[24]	IHC,WB
Anti-STAG3	HPA049106	IHC
Anti-SYNC	HPA028311	IHC,ICC-IF
Anti-TACC3	HPA005781[25]	IHC,WB
Anti-TBXAS1	HPA031257	IHC
Anti-TBXAS1	HPA031258	IHC
Anti-TBXAS1	HPA031259	IHC,WB
Anti-TGFBI	HPA017019	IHC,WB
Anti-TMEM154	HPA019184	IHC
Anti-TMEM222	HPA016579	IHC,ICC-IF
Anti-TMEM47	HPA046658	IHC,ICC-IF
Anti-TPX2	HPA005487[26]	IHC,WB,ICC-IF

12. MacDonald MJ *et al.* Mitochondrial malic enzyme (ME2) in pancreatic islets of the human, rat and mouse and clonal insulinoma cells. *Arch Biochem Biophys* 2009 Aug 15; 488(2):100-4.

13. MacDonald MJ *et al.* Mitochondrial malic enzyme (ME2) in pancreatic islets of the human, rat and mouse and clonal insulinoma cells. *Arch Biochem Biophys* 2009 Aug 15; 488(2):100-4.

14. MacDonald MJ *et al.* Mitochondrial Malic Enzyme (ME2) In Pancreatic Islets of the Human, Rat and Mouse and Clonal Insulinoma Cells: Simple Enzyme Assay For Mitochondrial Malic Enzyme 2. *Arch Biochem Biophys* 2009 Aug 15; 488(2):100-104.

15. 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.

16. 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

17. den Boon JA *et al.* Molecular transitions from papillomavirus infection to cervical precancer and cancer: Role of stromal estrogen receptor signaling. *Proc Natl Acad Sci U S A* 2015 Jun 23; 112(25):E3255-E3264. Epub 2015 Jun 8.

18. Laguë MN *et al.* Decidual PTEN expression is required for trophoblast invasion in the mouse. *Am J Physiol Endocrinol Metab* 2010 Dec; 299(6):E936-E946. Epub 2010 Sep 21.

19. 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.

20. 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.

21. 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.

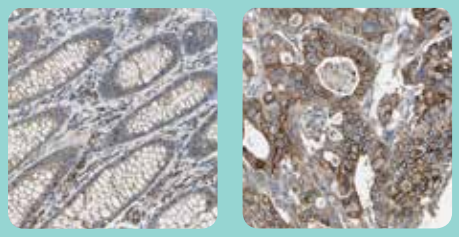
22. Ek S *et al.* From gene expression analysis to tissue microarrays: a rational approach to identify therapeutic and diagnostic targets in lymphoid malignancies. *Mol Cell Proteomics* 2006 Jun; 5(6):1072-81. Epub 2006 Mar 8.

23. Fagerberg L *et al.* Analysis of the Human Tissue-specific Expression by Genome-wide Integration of Transcriptomics and Antibody-based Proteomics. *Mol Cell Proteomics* 2014 Feb; 13(2):397-406. Epub 2013 Dec 5.

24. 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.

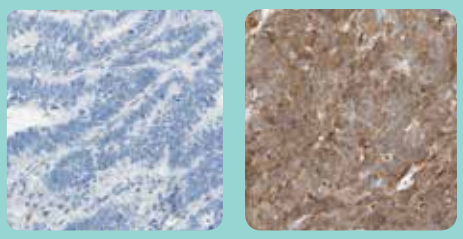
25. Guo Y *et al.* Regulating the ARNT/TACC3 axis: Multiple approaches to manipulating protein/protein interactions with small molecules. *ACS Chem Biol* 2013 Mar 15; 8(3):626-635. Epub 2012 Dec 26.

Anti-HEPH (HPA005824)



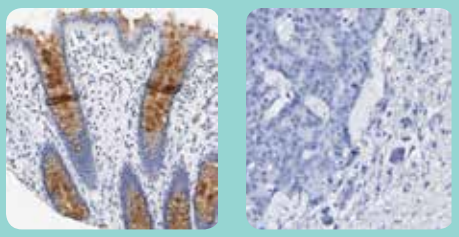
Using IHC, the Anti-HEPH antibody (HPA005824) shows cytoplasmic and membranous positivity in glandular cells in normal human colon tissue. In some colorectal cancer samples, prominent membranous positivity could be seen.

Anti-GLUL (HPA007316)



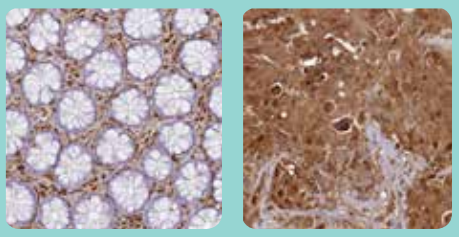
Using IHC, the Anti-GLUL antibody (HPA007316) shows either positive, or negative staining in different colorectal cancer samples.

Anti-SOCS7 (HPA004475)



The Anti-SOCS7 antibody (HPA004475) shows positivity in glandular cells in normal human colon tissue, while colorectal cancer samples are negative.

Anti-S100A4 (HPA007973)



The Anti-S100A4 antibody (HPA007973) shows no positivity in glandular cells in normal human colon tissue (left image), while colorectal cancer samples are either positive (right image), or negative.

Epithelial to Mesenchymal Transition Marker Panel

The EMT Panel

Epithelial and mesenchymal cells are fundamentally different and represent the two main cell types in the body. Epithelial cells are polarised along the apical/basal axis and are tightly connected to each other as well as to underlying basement membrane by a number of cell junction proteins. In contrast, mesenchymal cells are adhered to the extracellular matrix and have enhanced migratory capacities.

Epithelial cells can transition into mesenchymal cells – a process known as epithelial-mesenchymal transition (EMT), which leads to loss of epithelial barrier functions and changes in cell adhesion and motility[1]. Normally, EMT occurs during development (embryogenesis), but it is also present in wound healing and cancer progression of epithelial tumors. In metastasis, tumor cells dissociate from the epithelial layer, penetrate through basement membrane into connective tissue and can then enter the vascular system for further dissemination and subsequent growth of distant metastases[2].

A number of factors drive and regulate the EMT process, including zinc finger proteins such as SNAI1, SNAI2, ZEB1 and ZNF703. These transcription factors down-regulate the expression of epithelial cell adhesion proteins such as E-cadherin, occludin, beta-catenin and claudin. In addition, they up-regulate expression of mesenchymal proteins, including N-cadherin, fibronectin, vimentin, S100A4 and others. Taken together, EMT leads to increase motility and invasiveness of cancer cells[1].

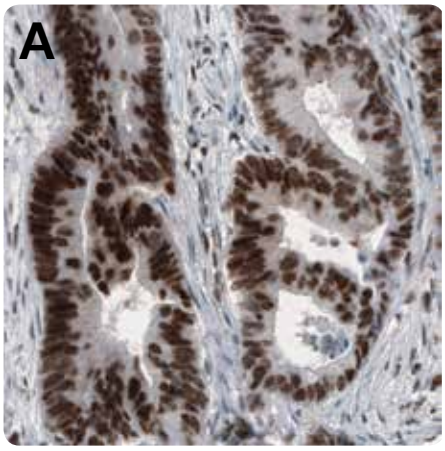
This panel of Prestige Monoclonals has been developed against the key EMT markers for cell junctions, cytoskeletal changes, transcription regulation and migration/motility. The antibodies targeting selected EMT marker proteins are:

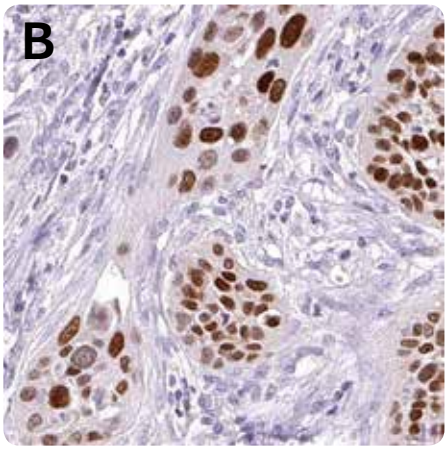
- IHC-validated in relevant normal and cancer human tissues
- WB-validated in positive and negative cell lines (when available)
- Available with different isotypes, allowing for multiplexing experiments
- Supplemented with information on antigens used for immunization and precise epitope sequence (when available)

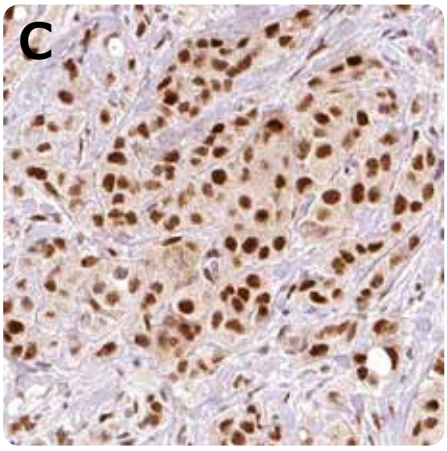
The monoclonal antibodies within the panel have been developed using the same stringent conditions as for all Prestige Monoclonals, ensuring a secured continuity and stable supply.

Using Monoclonals of Defined Isotypes for Multiplexed Immunofluorescence

The EMT panel includes monoclonal antibodies with different isotypes, which allows for co-localization studies using immunofluorescence with isotype-specific secondary antibodies. The images on the right side show multiplexed staining of colorectal cancer tissue derived from two different patients using the Anti-CDH1 (A, E: AMAb90863, IgG1), Anti-CTNNB1 (B, F: AMAb91209, IgG2a) and LAMC1 (C, G: AMAb91138, IgG2b) monoclonal antibodies, respectively. The tumor with higher degree of differentiation (indicated by preserved basement membrane, C) shows higher expression of E-cadherin (A) as compared to the tumor with lower differentiation grade (E). Also note the absence of LAMC1 immunoreactivity in the second tumor (G). Beta-catenin (CTNNB1) expression is preserved in both tumors (B, F). Panels D and H show overlay images for the two tumors.







Transcription factors involved in regulation of EMT. IHC images show nuclear immunoreactivity in tumor cells in (A) colorectal cancer (Anti-SNAI1 antibody AMAb91215), (B) cervical cancer (Anti-SIX1 antibody AMAb90544) and (C) breast cancer (Anti-ZNF703 AMAb90789).

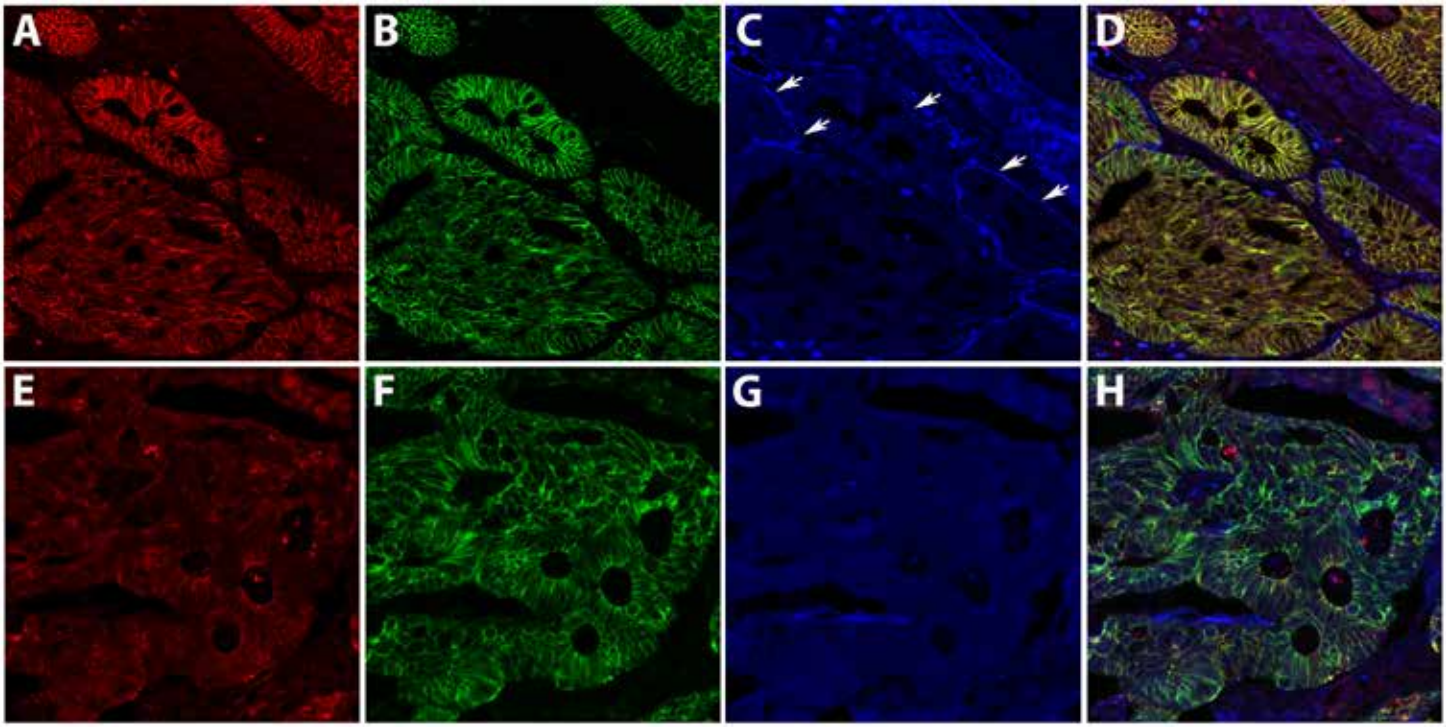
Table 1.
Summary of the Prestige Monoclonals EMT Markers.

Marker for	Product Name	Product Number	Validated Applications	Epitope	Isotype
Cell junctions	**Anti-CDH1**	AMAb90862	IHC, WB	NWTIQYNDPTQESII	IgG2b
Cell junctions	**Anti-CDH1**	AMAb90863	IHC, WB	APIPEPRTIF	IgG1
Cell junctions	**Anti-CDH1**	AMAb90865	IHC, WB	LKPKMALEVG	IgG2a
Cell junctions	**Anti-OCLN**	AMAb90889	IHC, WB	TSPVDDFRQPRYSSG	IgG2a
Cell junctions	**Anti-OCLN**	AMAb90890	IHC, WB	NDKRFYPESSYKSTP	IgG2a
Cell junctions	**Anti-OCLN**	AMAb90893	IHC, WB	RYSSGGNFETPSKRA	IgG1
Cell junctions	**Anti-CTNNB1**	AMAb91209	IHC, WB	TSQVLYEWEQGFSQS	IgG2a
Cell junctions	**Anti-CTNNB1**	AMAb91210	IHC, WB	TSQVLYEWEQGFSQS	IgG1
Cell junctions	**Anti-CLDN1**	AMAb91213	IHC, WB	KTTSYPTPRPYPKPA	IgG1
Cytoskeletal changes	**Anti-VIM**	AMAb90516	IHC, WB	N.D.	IgG1
Cytoskeletal changes	**Anti-S100A4**	AMAb90596	IHC, WB	KFKLNKSELKELLTR	IgG1
Cytoskeletal changes	**Anti-S100A4**	AMAb90598	IHC, WB	CNEFFEGFPDKQPRKK	IgG2b
Cytoskeletal changes	**Anti-S100A4**	AMAb90599	IHC, WB	CNEFFEGFPD	IgG1
Transcription regulation	**Anti-SNAI1**	AMAb91215	IHC	N.D.	IgG1
Transcription regulation	**Anti-ZEB1**	AMAb90510	IHC, WB, ICC	N.D.	IgG1
Transcription regulation	**Anti-SIX1**	AMAb90544	IHC, WB, ICC	N.D.	IgG1
Transcription regulation	**Anti-ZNF703**	AMAb90789	IHC, WB	PGDKAGFRVP	IgG1
Transcription regulation	**Anti-TP63**	AMAb91224	IHC, WB	MQYLPQHTIETYRQQ	IgG1
Migration/Motility	**Anti-CDH2**	AMAb91220	IHC, WB	ENPYFAPNPK	IgG1
Migration/Motility	**Anti-FN1**	AMAb91223	IHC, WB	GRWKCDPVDQ	IgG1
Migration/Motility	**Anti-MMP9**	AMAb90804	IHC, WB	VPDLGRFQTF	IgG1
Migration/Motility	Anti-MMP9	AMAb90805	IHC, WB	RGESKSLGPALLLLQ	IgG1
Migration/Motility	Anti-MMP9	AMAb90806	IHC	RGESKSLGPALLLLQ	IgG2b

Related Publications

1. Lamouille S *et al*. Molecular mechanisms of epithelial-mesenchymal transition. 2014 *Nat Rev Mol Cell Biol.* 15(3):178-196

2. Chambers AF *et al*. 2002. Dissemination and growth of cancer cells in metastatic sites. *Nat Rev Cancer* 2(8):563-572.



Multiplexed IHC-IF staining of two colorectal tumors (A-D and E-H) showing E-cadherin (A, E), beta-catenin (B, F) and laminin-gamma 1 (C, G) immunoreactivity using primary antibodies of different isotypes: Anti-CDH1 AMAb90863, IgG1 (red), Anti-CTNNB1 AMAb91209, IgG2a (green) and Anti-LAMC1 (AMAb91138), IgG2b (blue). Arrowheads in C indicate basement membrane. Alexa Fluor® 647-, 594- and 488-labelled isotype-specific secondary antibodies (Life Technologies) were used for visualisation.

Finding biomarkers for colorectal cancer research

Colorectal Cancer

Colorectal cancer is one of the most common types of cancer. Each year, approximately one million new cases are detected, and approximately 600,000 deaths can be contributed to this disease worldwide. Today, surgery is the only curative treatment for colorectal cancer, but adjuvant treatment may significantly improve patient survival. For adjuvant treatment to be successful, however, it is important to correctly identify patients that will benefit from treatment. For colon cancer, which accounts for approximately 70% of colorectal cancer cases, adjuvant treatment is currently recommended for patients with stage III and high-risk stage II disease. For patients with stage II colon cancer, it is thus of utmost importance to find biomarkers that can separate high-risk disease from low-risk disease.

Colorectal Cancer Biomarkers

Within the Human Protein Atlas (HPA) project, several potential prognostic and diagnostic biomarkers have been discovered. By staining of both normal- and tumor tissue samples, proteins with a tissue specific expression have been identified. Also, proteins with a differential expression in colorectal tissue samples from different patients have been identified. These potential biomarkers have subsequently been analyzed in larger patient cohorts, and their prognostic potential evaluated. Below, some of the most promising markers are described briefly.

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. During stress, RBM3 is thought to protect the cells by aiding in maintenance of protein synthesis needed for survival. Recently, it has also been shown that RBM3 attenuates stem cell-like properties in prostate cancer cells.

The RNA-binding protein RBM3 was identified via the Human Protein Atlas as an oncology biomarker through the differential expression pattern observed within several investigated cancers.

The levels of RBM3 expression were found to have a significant correlation to patient survival in breast, colon, ovarian, testicular, prostate and urothelial cancer as well as in malignant melanoma.

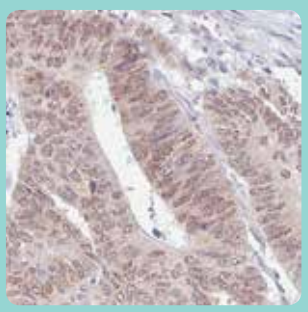
RBM3 as a prognostic biomarker in colon cancer

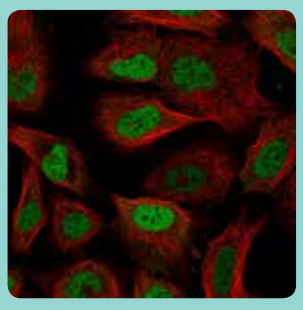
RBM3 was shown to be a prognostic marker in colorectal cancer in two independent patient cohorts, with a significantly improved survival for patients with high levels of RBM3 expression in their tumors. When analyzing stage II patients separately, similar results were obtained.

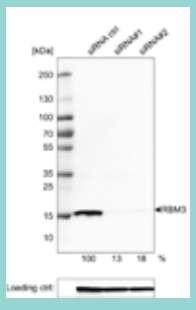
This indicates that RBM3 may be used as a biomarker for aid in deciding which stage II patients would benefit from adjuvant treatment.

RBM3 as a treatment predictive biomarker

The RBM3 protein has also been shown to be a treatment predictive marker for platinum based treatment. Chemotherapy with oxaliplatin is commonly used in colorectal cancer treatment.







The Anti-RBM3 (AMAb90655) antibody shows nuclear positivty by IHC in cancer cells in human colorectal tumor samples and nuclear staining by ICC-IF in U2-OS cells. By WB, the AMAb90655 antibody signal is down regulated using target specific siRNA probes in U-251 cells.

Related Publications

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.* Jul 1;73(13):4123-33.

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.

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.

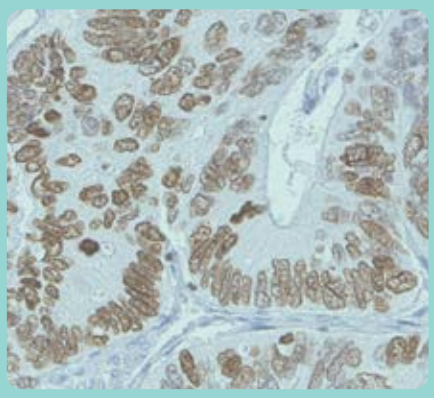
Boman K *et al*. Decreased expression of RNA-binding motif protein 3 correlates with tumour progression and poor prognosis in urothelial bladder cancer. *BMC Urol.* 2013, 13:17.

SATB2 – A diagnostic biomarker for tumors of colorectal origin

Cell- and cancer-type specific proteins are rare. The special AT-rich sequence-binding protein SATB2 has been identified as having a very selective expression pattern. In cells of epithelial lineages, SATB2 is expressed in glandular cells lining the lower gastrointestinal tract and expression is retained in a large majority of primary and metastatic colorectal cancers. Thus, SATB2 is a promising diagnostic biomarker for tumors of colorectal origin.

In a previously published study by Magnusson et al it was shown, by analyzing more than 1,800 tumor samples, that SATB2 expression is largely preserved in cells of colorectlal cancer origin. More than 85% of all colorectal cancers showed distinct SATB2 immunostaining and when used in combination with Cytokeratin 20 analysis, SATB2 identified more than 95% of all tumors with colorectal origin.

These promising data suggested that the combination of SATB2 and CK20 should be tested in an unbiased clinical study to further validate the initial findings. In a recent publication by Dragomir et al, the expression of SATB2 was analyzed in over 800 consecutive clinical cases for which CK20 immunostaining was considered necessary to obtain a final diagnosis. In this study, SATB2 showed 93% sensitivity and 77% specificity to determine a cancer of colorectal origin and in combination with CK7 and CK20, the specificity increased to 100%. SATB2 thus provides a new and advantageous supplement to current standards for clinical differential diagnosis.



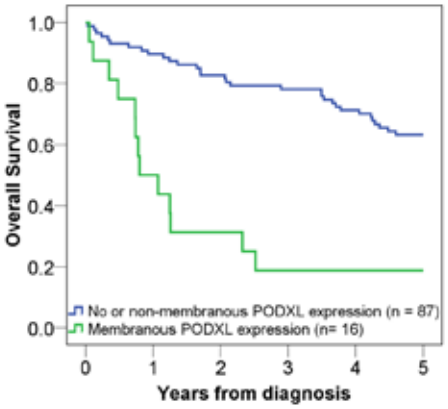
Immunohistochemical staining of human colorectal tumor with Anti-SATB2 antibody (AMAb90635) shows strong nuclear staining in tumor cells.

Related Publications

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.

Dragomir A *et al*. The role of SATB2 as a diagnostic marker for tumors of colorectal origin: results from a pathology-based clinical prospective study. *Am J Clin Pathol.* 2013 In press.

PODXL - An independent factor for poor prognosis and treatment stratification

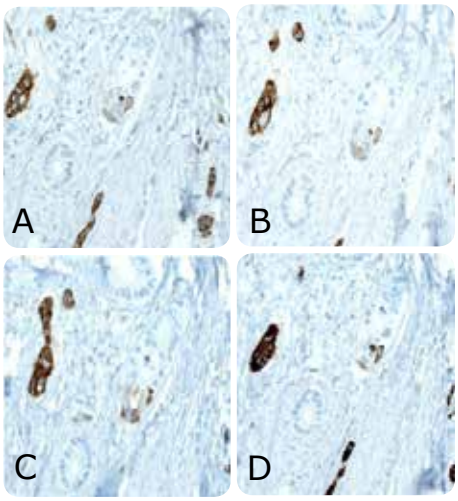


Kaplan–Meier estimates of 5-year Overall Survival (OS) according to PODXL expression in a urothelial cancer patient cohort of 110 individuals.

Podocalyxin-like 1 (PODXL) is a cell-adhesion glycoprotein and stem cell marker that has been associated with aggressive tumor phenotype and adverse outcome in several cancer types.

In a number of recently published papers, Larsson *et al* have demonstrated that membraneous expression of PODXL is associated with unfavourable clinicopathological characteristics and independently predicts a poor prognosis in colorectal cancer (CRC). This has been demonstrated in three independent patient cohorts in total comprising more than 1,000 patients. The results clearly demonstrate the potential utility of PODXL as a biomarker for more precise prognostication and treatment stratification in CRC.

Boman *et al* have investigated the prognostic impact of membraneous PODXL expression in almost 500 cases of urothelial cancer. They concluded that PODXL is indeed an independent risk factor for progressive disease and death in patients with urothelial cancer and that this warrant further studies to fully evaluate the use of PODXL as a biomarker for improved treatment stratification of bladder cancer patients.



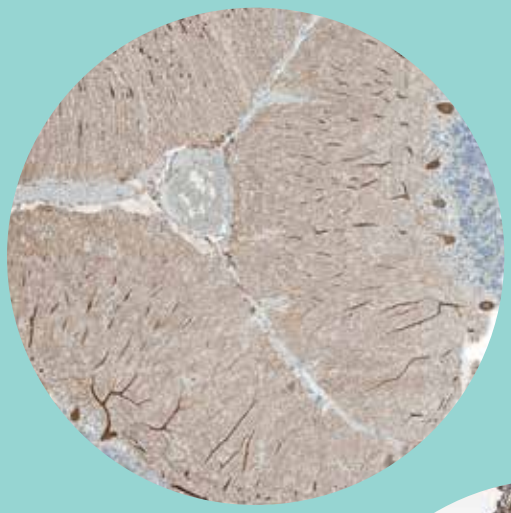
Immunohistochemical staining of PODXL protein in colorectal tumor tissue using A) HPA002110, B) AMAb90643, C) AMAb90644 and D) AMAb90667 antibodies.

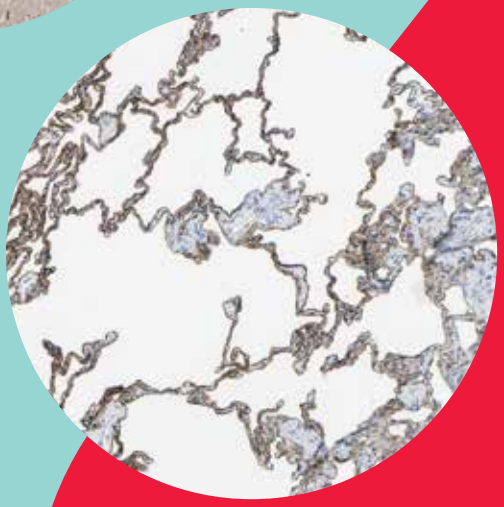
Related Publications

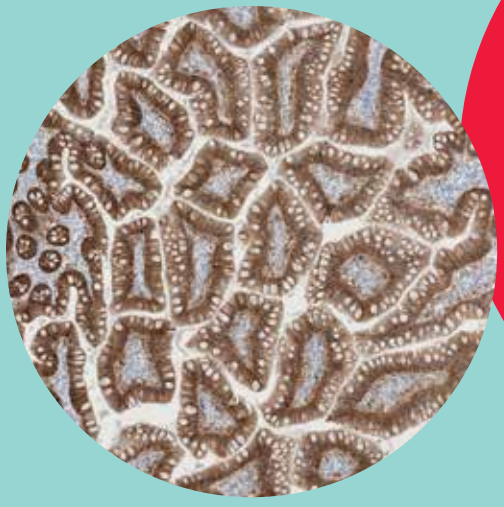
Larsson A *et al*. Overexpression of podocalyxin-like protein is an independent factor of poor prognosis in colorectal cancer. *Br J Cancer* 2011 Aug 23;105(5):666-72.

Larsson A *et al*. Validation of podocalyxin-like protein as a biomarker of poor prognosis in colorectal cancer. *BMC Cancer.* 2012 Jul 8;12:282.

Boman K *et al*. Membraneous expression of podocalyxin-like protein is an independent factor of poor prognosis in urothelial bladder cancer. *Br J Cancer.* 2013 Jun 11;108(11), 2321-2328.







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