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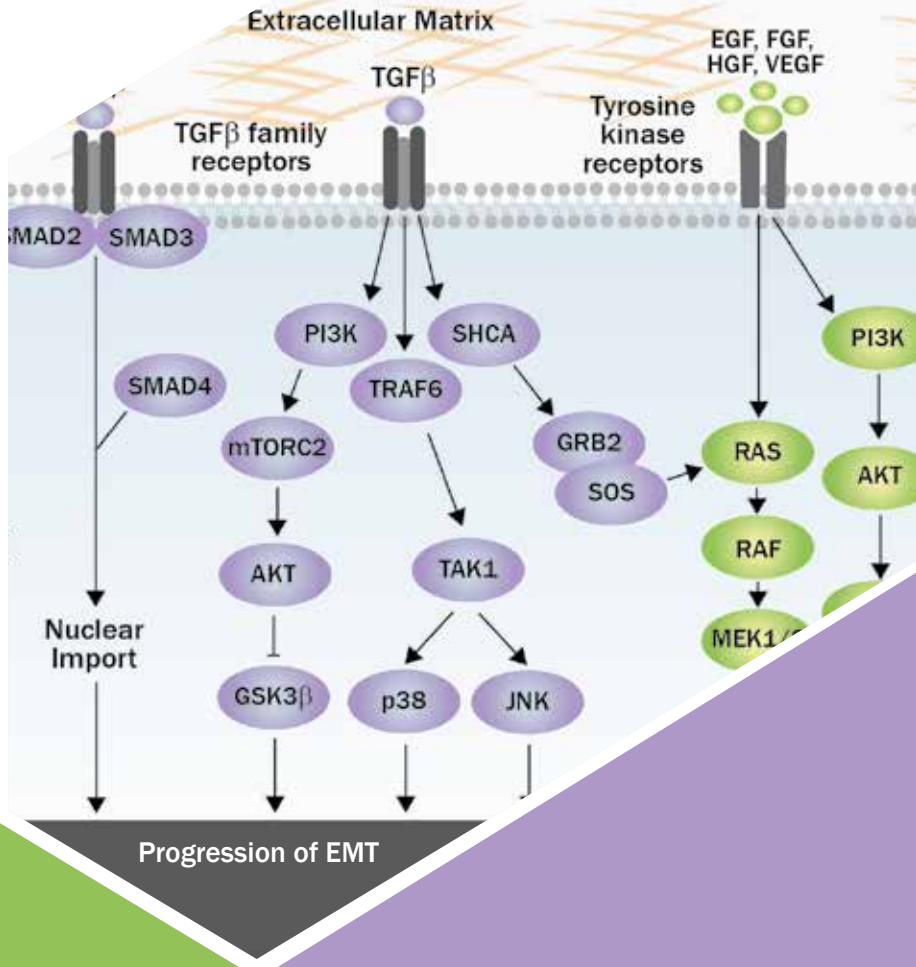
Antibodies for Epithelial-Mesenchyal Transition (EMT)



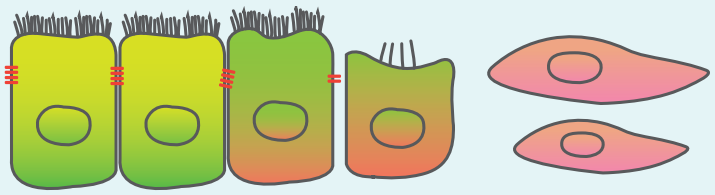
INTRODUCTION

Epithelial-mesenchymal transition (EMT) refers to the trans-differentiation of stationary epithelial cells into motile mesenchymal cells. Major changes which occur during EMT are the down-regulation of epithelial proteins (such as E-Cadherin, TJP1/ZO-1 and Occludin), rearrangement of the cytoskeleton, loss of cell-cell adhesion and apical-basal polarity, and the acquisition of mesenchymal proteins (such as Vimentin, N-Cadherin and Fibronectin). Mesenchymal-epithelial transition (MET) is the reverse process of EMT. A coordination of EMT and MET signals is fundamental to a wide range of biological processes including primary/secondary epithelia generation during embryogenesis or organogenesis, wound healing, and to the pathophysiology of fibrosis and malignancies.

In transcriptional control of EMT, the mesenchymal phenotype is driven by the factors: SNAI1/Snail, ZEB and bHLH proteins (refer to graphics of transcription factors pathway on page 1). The activities of these transcription factors are regulated through their post-translational modification, subcellular localization, and stability. Specifically, GSK-3 beta and/or PKD1 (PKC mu) phosphorylates SNAI1 triggering its nuclear export and subsequent degradation via the ubiquitin (Ub)-proteasome pathway. SNAI1's nuclear retention and signaling activity are promoted through its phosphorylation by PAK1 or LATS2, or its de-phosphorylation by SCP1. SNAI2/Slug, a repressor of E-Cadherin/CDH1, gets degraded upon p53-mediated recruitment to the MDM2 complex. Transcriptional regulator TWIST's nuclear translocation/activity is controlled through its phosphorylation by MAPK p38, JNK and ERK. ZEB2, another inhibitor of E-Cadherin, gets sumoylated by PRC2 and this modification leads to its translocation into the cytoplasm which reduces its activity.

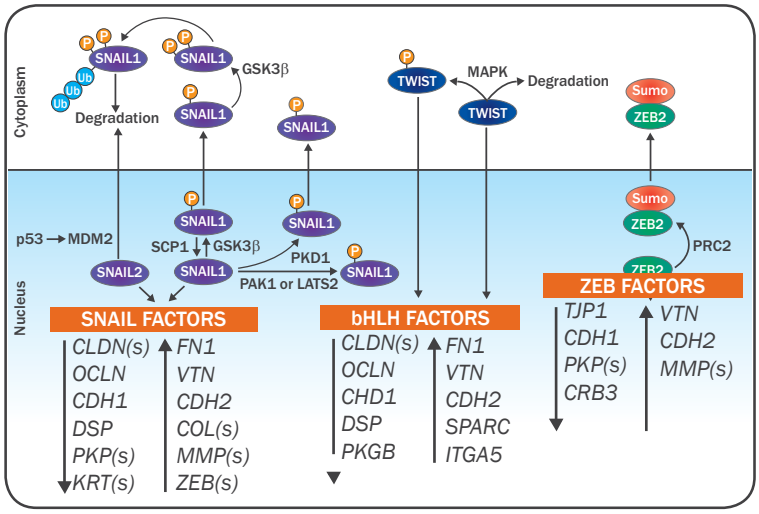
At the molecular level, EMT is regulated via multiple signaling pathways (refer to graphics of major signaling pathways on page 1). TGF-beta, the most studied EMT-signaling molecule, interacts with Type I/II receptors to activate SMAD2/3, resulting in the formation of the SMA2/3/4 complex. Upon nuclear translocation, this complex interacts with transcription factors responsible for controlling genes favoring the EMT phenotype. Additionally, TGF-beta impacts the induction of miRNAs which are known to down-regulate the expression of epithelial markers. TGF-beta induces PI3K-AKT, ERK-MAPK, p38-MAPK and JNK signaling for controlling EMT rogression. TGF-beta type 1 receptor phosphorylates SHCA which generates a docking site for GRB2 and SOS, activating RAS-RAF-MEK-ERK MAPK signaling. TGF beta receptor complex-TRAF6 interaction activates TAK1 which further induces p38 MAPK and JNK, and leads to EMT progression. Upon stimulation by growth factors (EGF, FGF, HGF and VEGF), receptor tyrosine kinases (RTKs) activate RAS-RAF-MEK-ERK MAPK signaling cascade. Activated ERK1/2-MAPK induces key transcription factors, as well as EMT promoting regulators of cell motility and invasion (RHO GTP-ases and S6K). Wnt signaling is known to drive EMT through GSK3 beta inhibition, beta-catenin stabilization and TCF-LEF mediated activation of the EMT program. RTKs or integrin induced AKT activation leads to increase in the expression of SNAI1 via inhibition of GSK-3 beta. GLI1 induces SNAI1 (Snail) expression in Hedgehog signaling, while SNAI2 (Slug) expression is up-regulated by the intracellular domain of Notch, which can lead to a decreased E-cadherin expression (a hallmark of EMT). IL6 and other inflammatory cytokines secreted by cancer cells promote EMT via STAT3-induced SNAI1/Snail expression. In hypoxic tumor microenvironment, HIF-1 alpha activates the expression of TWIST which ultimately induces EMT.

Epithelial and Mesenchymal Markers

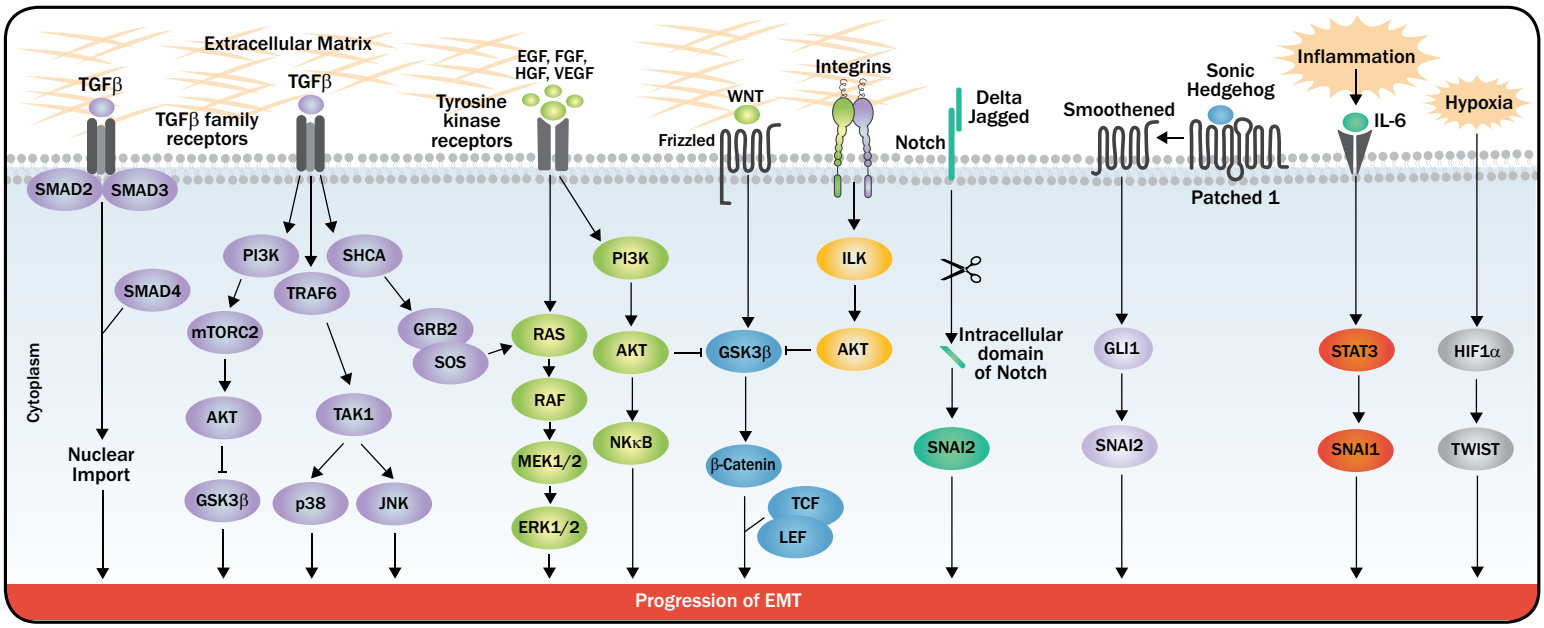


Epithelial Markers		Mesenchymal Markers	
E-cadherin	Syndecan	N-cadherin	Snail
Cytokeratin	MUC1	Vimentin	Slug
TJP1/ZO-1	Desmoplakin	Fibronectin	ETS1
Laminin-1	COL4A1	OB-cadherin	a-SMA
Entactin	collagen	a5b1 integrin	Twist

Transcription Factors Involved in EMT



Major Signaling Pathways Driving the Progression of EMT

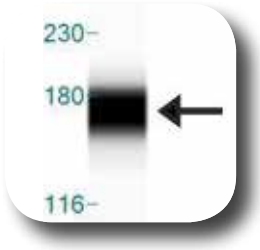


Novus Biologicals offers extensively validated high quality antibodies for various epithelial and mesenchymal markers, and for critical players of EMT signaling.

Epithelial Marker
pan Cytokeratin Antibody
NBP2-29429 (29 publications)

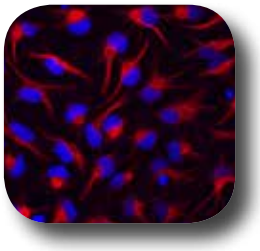
IHC-P analysis of formalin-fixed human colon carcinoma section using pan Cytokeratin antibody (clone AE1+AE3).

Mesenchymal Marker
ZEB1 Antibody
NBP1-05987 (24 publications)



Simple Western analysis of 0.5 mg/ml Jurkat lysate on 12-230 kDa separation system using ZEB1 Antibody.

Mesenchymal Marker
Vimentin Antibody
MAB2105 (12 publications)

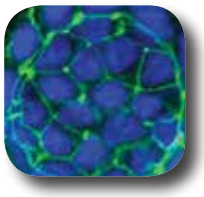


Confocal staining analysis of mixed neuron/glial cultures with NB300-223 (green) and GFAP antibody NB300-141 (red).

Epithelial Phenotype Markers

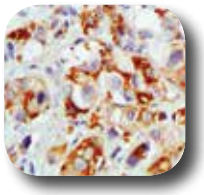
Target	Catalog#	Host/Clonality	Species	Applications
Claudin-1	NBP1-67515	Rb/Poly	Hu, Mu, Rt	WB, ELISA, ICC/IF, IHC-P
COL4A1	NB120-6586	Rb/Poly	Hu, Mu, Rt, Bv, Ma	WB, ELISA, IHC-P, IP
pan Cytokeratin	NBP2-29429	Mu/Mono	Hu, Mu, Rt, Bv, Ca, Ch, Pm, Rb	WB, Flow, ICC/IF, IHC-Fr, IHC-P
Cytokeratin 1	NB100-2756	Mu/Mono	Hu, Rt	WB, ICC/IF, IHC-Fr, IHC-P
Cytokeratin 18	NBP2-29461	Mu/Mono	Hu	SW, WB, ELISA, Flow, ICC/IF, IHC-Fr, IHC-P, IP
Desmocollin-1	NBP1-88099	Rb/Poly	Hu	SW, WB, IHC-P
Desmoglein 3	NBP1-78984	Mu/Mono	Hu	WB, ICC/IF, IHC-P, IP
Desmoplakin	NBP1-49879	Gt/Poly	Hu	WB, IHC-P, PEP-ELISA
E-Cadherin	NBP2-19051	Mu/Mono	Hu, Mu, Rt, Pm	WB, ELISA, Flow, ICC/IF, IHC-P
Laminin	NB300-144	Rb/Poly	Hu, Mu, Rt, Rb, Sh	WB, Func, ICC/IF, IHC-Fr, IHC-P
MUC-1	NB120-22711	Mu/Mono	Hu, Mu	ELISA, ICC/IF, IHC-Fr, IHC-P
Nidogen-1	NBP2-16341	Rb/Poly	Hu	WB, IHC-P
Occludin	NBP1-77037	Rb/Poly	Hu, Mu, Rt	WB, ELISA, ICC/IF, IHC-P
Syndecan-1	NB100-64980	Mu/Mono	Hu	WB, Flow, Func, ICC/IF, IHC-Fr, IHC-P
TJP1/ZO1	NBP1-85046	Rb/Poly	Hu	ICC/IF, IHC-P

E-Cadherin Antibody
NBP2-19051 (3 publications)



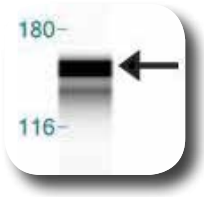
Confocal staining analysis of human colon cancer sphereroids using E-Cadherin antibody (clone 7H12) with DyLight 488 labelled secondary and DAPI counterstaining.

MUC-1 Antibody
NB120-22711 (11 publications)



IHC-P analysis of human breast cancer xenograft tissue using MUC-1 antibody with HRP-DAB detection and hematoxylin counterstaining.

N-Cadherin Antibody
NBP1-48309 (20 Publications)

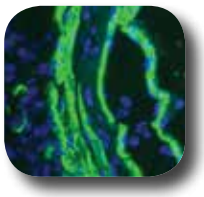


Simple Western analysis of 1.0 mg/ml of HeLa lysate with N-Cadherin antibody using 12-230 kDa separation system.

Mesenchymal Phenotype Markers

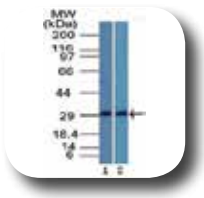
Target	Catalog#	Host/Clonality	Species	Applications
alpha SMA	NB600-531	Rb/Poly	Hu, Mu, Rt	WB, ICC/IF, IHC-Fr, IHC-P
alpha SMA	NBP2-33006	Mu/Mono	Hu, Mu, Rt, Po, Bv, Ca, Ch, Fe, Gt, FP, Mk, Rb, Sh	WB, SW, ELISA, Flow, ICC/IF, IHC-Fr, IHC-P, IP
Fibronectin	NBP1-91258	Rb/Poly	Hu, Mu	SW, WB, ICC/IF, IHC-P
N Cadherin	NBP1-48309	Mu/Mono	Hu, Mu, Rt	SW, WB, ICC/IF, IHC-P, IP
N-Cadherin	NB200-592	Rb/Poly	Hu, Mu, Rt, Am, Av, Bv, Ca, Ch, Fi, Rb, Xp	WB, ICC/IF, IHC-Fr, IHC-P
OB-Cadherin	NBP1-00963	Rb/Poly	Hu, Mu, Rt	WB
S100A4	NBP2-36430	Mu/Mono	Hu	WB, ICC/IF, IHC-P
Slug	NBP2-27182	Rb/Poly	Hu, Ca, Eq	WB, IHC-P
Snail	NBP2-27184	Rb/Poly	Hu, Mu, Ca, Eq	WB, ICC/IF
Snail	NBP2-27293	Rb/Poly	Hu	SW, IHC-P
Snail (pS246)	NBP1-51411	Rb/Poly	Hu, Mu, Rt	WB, IHC-P
Vimentin	NB300-223	Ck/Poly	Hu, Mu, Rt	WB, ICC/IF, IHC-Fr, IHC-P
Vimentin	NBP1-92687	Mu/Mono	Hu, Mu, Rt, Ma	SW, WB, ICC/IF, IHC

alpha-Smooth Muscle Actin Antibody
NBP2-33006 (6 publications)



IHC analysis of a fozen section of human small intestine tissue using alpha - SMA antibody.

Snail Antibody
NBP2-27184

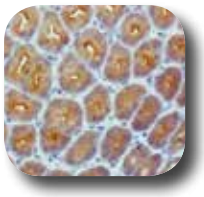


WB analysis of lysates from (1) murine D3 and (2) human MCF7 cell lines using Snail antibody.

Other Important Targets from EMT Signaling

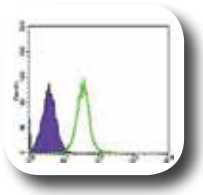
Target	Catalog#	Host/Clonality	Species	Applications
AKT1	NB100-56631	Rb/Poly	Hu	WB, ICC/IF
AKT1/2 (p er473)	NB100-56749	Mu/Mono	Hu, Mu	WB
beta-Catenin	NBP1-54467	Mu/Mono	Hu, Mu, Rt, Ch, Pm	SW, WB, ICC/IF, IHC-P, IP
beta-Catenin (pS33, pS37)	NB300-272	Rb/Poly	Hu	WB
COX-2	NB100-689	Rb/Poly	Hu, Mu, Rt	SW, WB, IHC-P
Dicer	NB200-591	Rb/Poly	Hu, Mu	WB, IHC-P
Ets-1	NB100-56620	Rb/Poly	Hu	WB
FBXL14	NBP2-33296	Rb/Poly	Hu	WB, ICC/IF, IHC-P
FoxC1	NBP2-24834	Rb/Poly	Hu, Pm	WB, IHC-P
FoxC2	NB100-1269	Gt/Poly	Hu, Mu	WB, ICC/IF, IHC-Fr, PEP-ELISA
GLI-1	NBP2-24662	Rb/Poly	Hu, Mu, Pm	WB, ICC/IF, IHC-P
Goosecoid	NBP2-37366	Mu/Mono	Hu	WB, ELISA, Flow, IHC-P
GSK-3 beta	NBP1-47470	Mu/Mono	Hu, Mu, Rt, Pm	SW, WB, ELISA, Flow, ICC/IF, IHC-P
GSK-3 beta (pS9)	AF1590	Rb/Poly	Hu, Mu, Rt	WB, ICC/IF, Flow
HDAC1	NB100-56340	Rb/Poly	Hu, Mu	SW, WB, IHC-P
HDAC2	NBP2-03980	Rb/Poly	Hu, Mu, Rt	WB, ICC/IF, IHC-P
HIF-1 alpha	NB100-131	Mu/Mono	Hu, Mu, Rt, Bv, Ca	SW, WB, ICC/IF, IHC-Fr, IHC-P, IP
ID2	NBP2-27194	Rb/Poly	Hu, Rt, Bv, Ch, Eq, Ha, Pm	WB, ICC/IF
ILK	NBP2-37448	Mu/Mono	Hu, Mu, Pm	WB, ELISA, Flow, IHC-P
ITGA5	NB100-78108	Mu/Mono	Hu	ELISA, Flow, IHC-Fr, IP
ITGB3	NB100-2680	Mu/Mono	Hu, Rt	Flow, ICC/IF, IHC-Fr, IP
KAP1	NB500-158	Rb/Poly	Hu, Mu	WB, ICC/IF, IHC-P, IP, PLA
KLF8	NBP2-27418	Rb/Poly	Hu, Pm	WB
LEF1	NB100-41374	Gt/Poly	Hu, Mu, Rt	WB, PEP-ELISA
MDM2	NB100-2736	Mu/Mono	Hu, Rt	WB, IHC-Fr, IHC-P, IP
MMP-2	NB200-193	Rb/Poly	Hu, Mu, Rt, Ch	WB, Flow, ICC/IF, IHC-Fr, IHC-P
MMP-2	NB200-114	Mu/Mono	Hu, Mu, Rt	WB, ELISA, ICC/IF, IHC-Fr, IHC-P, IP
MMP-3	NB100-91878	Rb/Poly	Hu, Mu, Rt	WB, IHC-P
MMP-7	NBP1-99123	Rb/Poly	Hu, Mu	IHC-P
MMP-9	NBP2-13173	Mu/Mono	Hu, Rt	WB, ELISA, IHC-P
Nanog	NBP2-24941	Rb/Poly	Hu, Mu, Gt, Pm	WB, ICC/IF
Notch-1	NB100-78486	Mu/Mono	Hu, Mu	WB, Flow, ICC/IF, IHC-P, IP
Notch-1	NBP1-78292	Rb/Poly	Hu, Mu	SW, WB, ICC/IF, IHC-P
p38	NB100-56665	Rb/Poly	Hu	WB, IHC-P
p38 (pTh180/Ty182]	NB500-138	Rb/Poly	Hu	WB, IHC-P
PALS1	NB300-952	Gt/Poly	Hu	WB, IHC-P, PEP-ELISA

beta-Catenin Antibody
NBP1-54467 (6 publications)



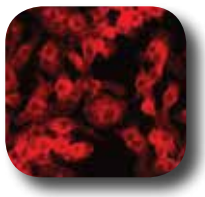
IHC analysis of mouse intestine section using beta-Catenin antibody with DAB detection and hematoxylin counterstaining.

GSK3 beta Antibody
NBP1-47470 (2 Publications)



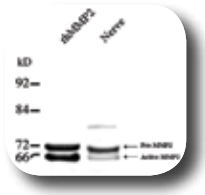
Flow analysis of Hela cells using GSK3 beta antibody (green) and a negative control (purple).

HIF-1 alpha Antibody (ESEE122)
NB100-131 (56 publications)



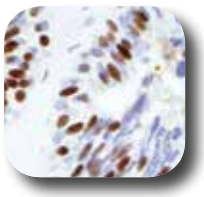
Confocal staining analysis of RAW264.7 cells using HIF-1 alpha antibody (clone ESEE122).

MMP-2 Antibody
NB200-193 (35 publications)



WB analysis of recombinant pro/active Human MMP-2 protein (left lane) and Rat's nerve lysate (right lane) using MMP-2 antibody.

KAP1 Antibody
NB500-158 (16 publications)

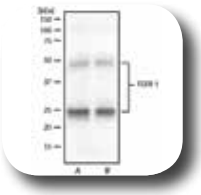


IHC-P analysis of a human prostate carcinoma tissue section using KAP1 antibody.

Other Important Targets from EMT Signaling Cont'd.

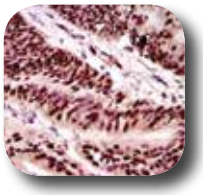
Target	Catalog#	Host/Clonality	Species	Applications
PATJ	NB100-1354	Gt/Poly	Hu	WB, IHC-P, PEP-ELI-SA
PDK-1	NB100-2383	Rb/Poly	Hu	WB, ICC/IF
Smad4	NBP2-24951	Rb/Poly	Hu, Mu, Rt, Pm	WB
SNAI3	NBP2-20433	Rb/Poly	Hu	WB, ICC/IF
SPARC	NBP1-80971	Rb/Poly	Hu	WB, IHC-Fr, IHC-P
STAT3	NBP2-22471	Mu/Mono	Hu, Mu, Rt, Pm	WB, ICC/IF, IHC-P, IP
SUMO2	NB100-56444	Rb/Poly	Hu, Mu	WB, IHC-P
TAZ/WWTR1	NB110-58359	Rb/Poly	Hu, Mu, Rt	WB, SW, ChIP, ICC/IF, IHC-P, IP
TGF-beta 1	NBP2-22114	Mu/Mono	Hu, Mu	WB, ELISA, Flow, IHC-P
TGF-beta (pan)	NBP2-45137	Mu/Mono	Hu, Mu, Rt, Bv, Ca, Ha, Mk	IHC-P
TGF-beta RI	MAB5871	Rt/Mono	Hu, Mu	WB
TGF-beta RII	NB100-91994	Rb/Poly	Hu, Mu, Rt	WB, ICC/IF, IHC-Fr, IHC-P
TIMP-1	NB100-74551	Mu/Mono	Hu, Mu	WB, ICC/IF, IHC-P
TIMP-2	NB100-92000	Rb/Poly	Hu, Mu, Rt	WB, ICC/IF, IHC-P
TRAF-6	NB100-56436	Rb/Poly	Hu, Mu, Rt, Bv	WB, IHC-P, IP
Twist-1	NBP2-37364	Mu/Mono	Hu, Mu	WB, ELISA, Flow, ICC/IF, IHC-P
Twist-2		Mu/Mono	Hu	WB, ELISA, IHC-P,
Vitronectin	NBP1-42299	Mu/Mono	Hu	WB, ELISA, IHC-Fr
Wnt-5a	NBP2-24752	Rb/Poly	Hu, Mu, Rt, Bv, Pm	WB, IHC-P
YAP1	NB110-58358	Rb/Poly	Hu, Mu	SW, WB, ChIP, ICC/IF, IHC-P, IP
YAP1	NBP2-22117	Mu/Mono	Hu	WB, ELISA, Flow, IHC-P
ZEB1	NBP1-05987	Rb/Poly	Hu, Mu	SW, WB, GS, ICC/IF, IHC-P, IP
ZEB1	NBP2-23484	Mu/Mono	Hu, Rt	WB, Flow, ICC/IF, IHC-P
ZEB2	NBP1-82991	Rb/Poly	Hu, Mu	ICC/IF, IHC-P

TGF-beta 1 Antibody
NBP2-22114 (2 publications)



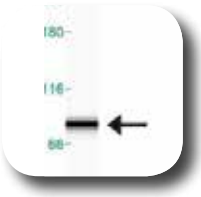
WB analysis of (A) human stomach and (B) small intestine tissue lysates with TGF beta 1 antibody.

Twist-1 Antibody
NBP2-37364



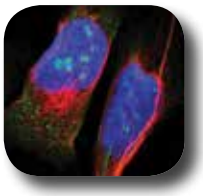
IHC-P analysis of a human colon cancer tissue using TWIST1 antibody with HRP-DAB detection.

YAP1 Antibody
NB110-58358 (10 publications)



Simple Western analysis of 0.1 mg/ml HeLa lysate on 12-230kDa separation system using YAP1 antibody.

ZEB2 Antibody
NBP1-82991 (7 publications)



Confocal staining analysis of human cell line U-2 OS using ZEB2 antibody.

Species Key: Am (Amphibian) Av (Avian), Bv (Bovine), Ca (Canine), Ch (Chicken), Eq (Equine), Fe (Feline), Fi (Fish), Gp (Guinea Pig), Gt (Goat), Ha (Hamster), Hu (Human), Ma (Mammals), Mu (Mouse), Pm (Non-human Primates), Po (Porcine), Rb (Rabbit), Rt (Rat), Sh (Sheep), Xp (Xenopus)

Applications Key: ChIP (Chromatin Immunoprecipitation), GS (Gel Super Shift Assay), ELISA (ELISA Capture and/or Detection), Flow (Flow Cytometry), Func (Functional), ICC/IF (Immunocytochemistry/Immunofluorescence), IHC-Fr (Immunohistochemistry-Frozen), IHC-P (Immunohistochemistry-Paraffin), IP (Immunoprecipitation), MiAr (Microarray), PEP-ELISA (Peptide ELISA), PLA (Proximity Ligation Assay), SW (Simple Western), WB (Western blot)

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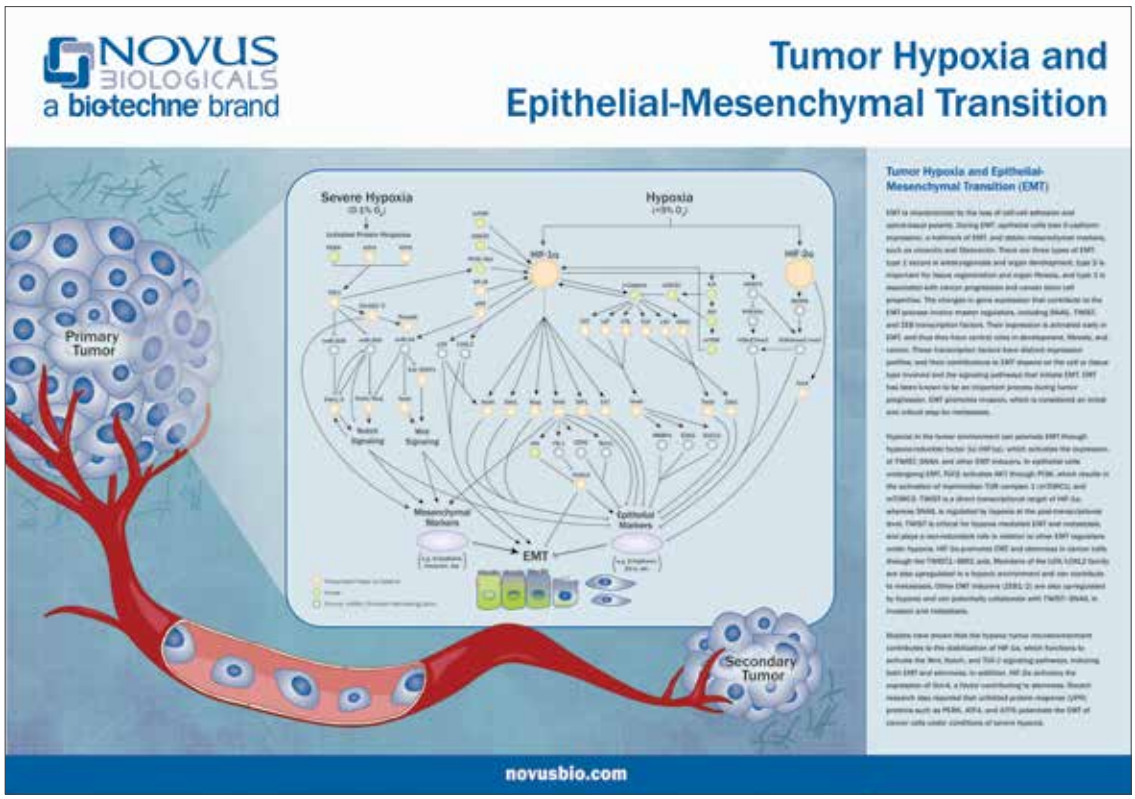
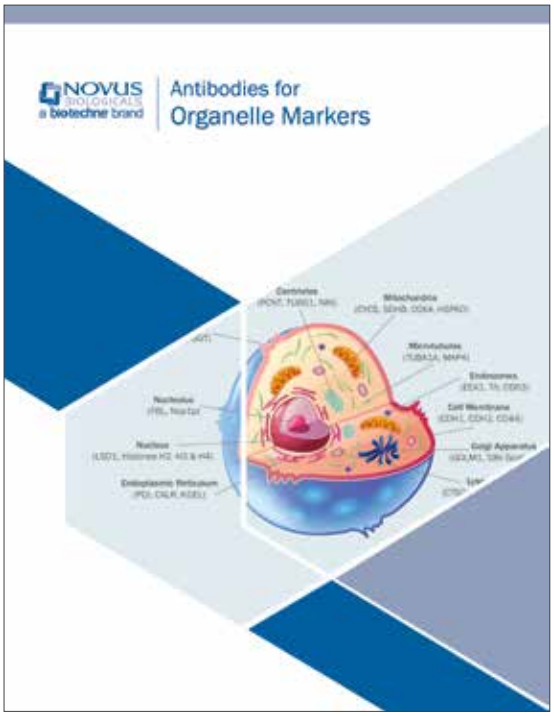
Tumor Hypoxia and EMT Poster



Exosome Research Tools

Organelle Markers



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