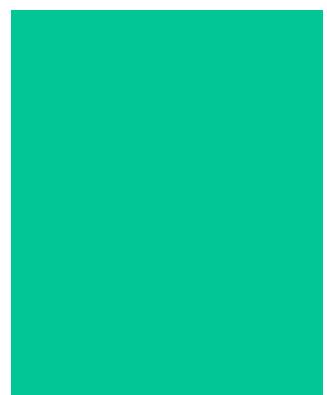


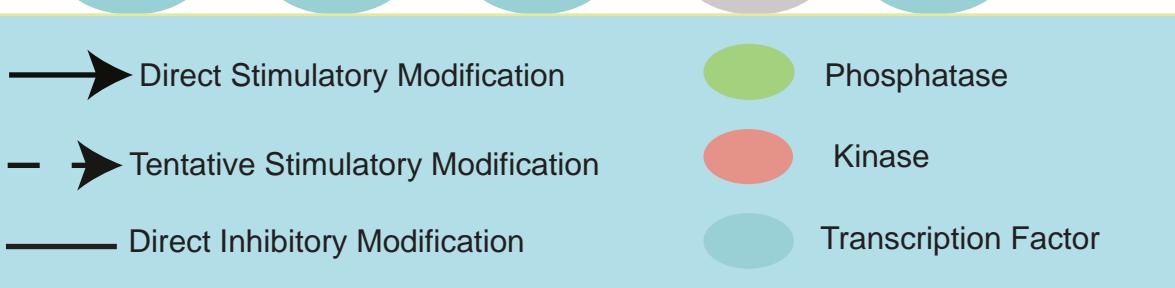
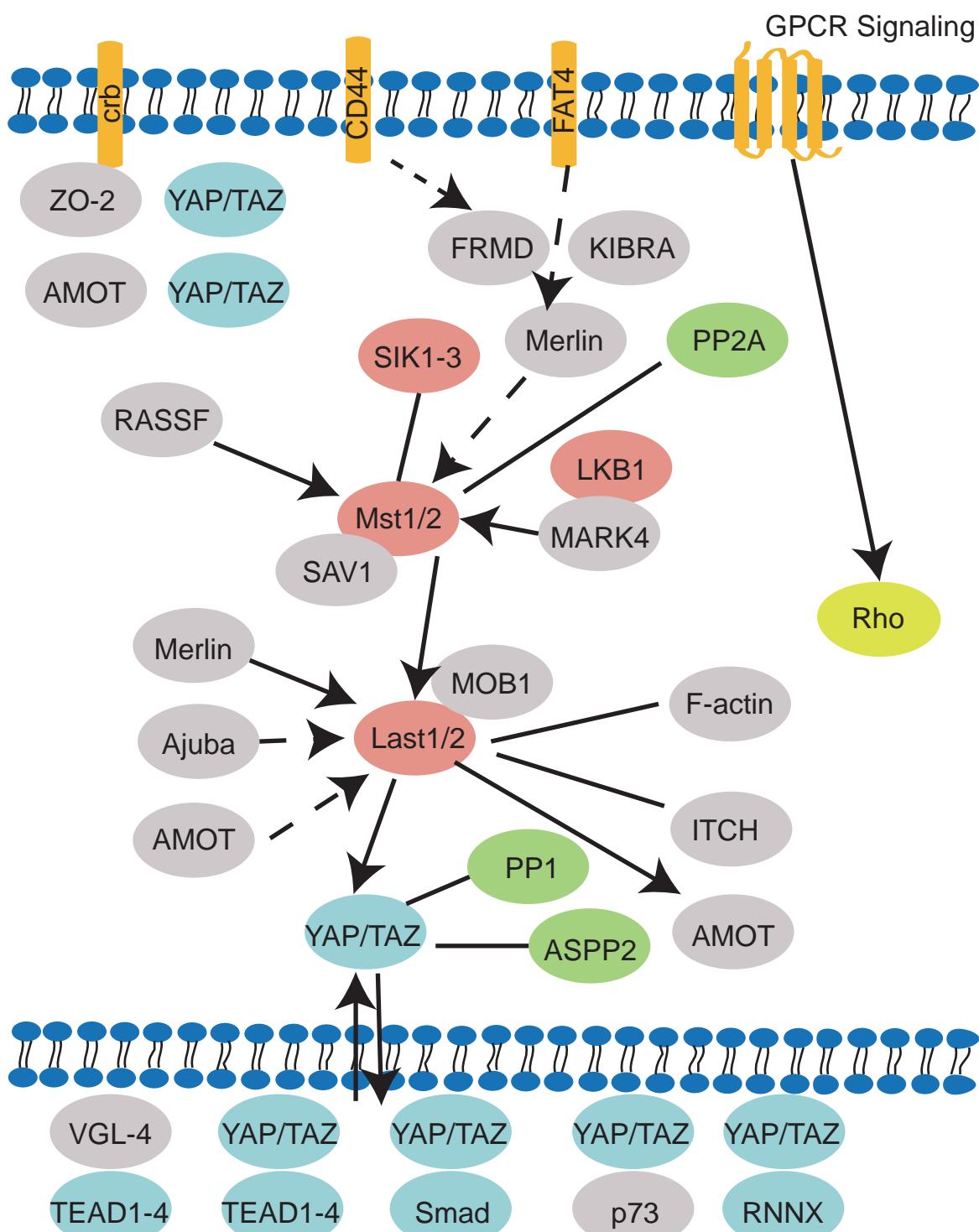
# Hippo Signal Pathway



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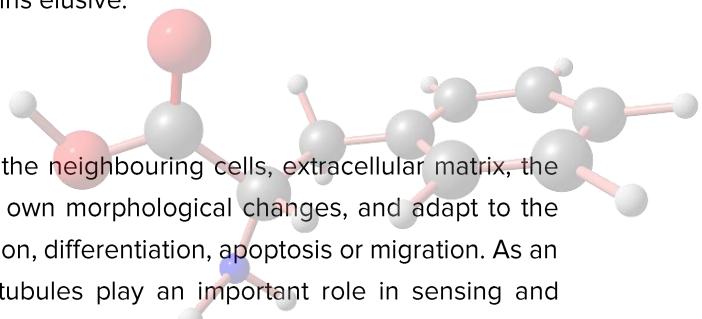
## Hippo Signal Pathway



## Introductions

Hippo signaling is an evolutionarily conserved pathway that can control organ size by regulating cell proliferation, apoptosis, and stem cell self-renewal. In addition, dysregulation of the hippo pathway leads to the development of cancer. The core of the hippo pathway is the kinase cascade, in which Mst1/2 (ortholog of Drosophila hippocampus) kinase and SAV1 form a complex to phosphorylate and activate LATS1/2. LATS1/2 kinase in turn phosphorylates and inhibits transcription coactivators YAP and TAZ, which are the two major downstream effectors of the hippo pathway. When dephosphorylated, YAP/TAZ translocates into the nucleus and interacts with TEAD1-4 and other transcription factors to induce gene expression that promotes cell proliferation and inhibits apoptosis. The Hippo pathway is involved in cell contact inhibition, and its activity is regulated at multiple levels: Mst1/2 and LATS1/2 are regulated by upstream molecules such as Merlin, KIBRA, RASSFs, and Ajuba. 14-3-3,  $\alpha$ -catenin, AMOT, and ZO-2 retain YAP/TAZ in the cytoplasm, adhesion junction, or tight junction by combining. The phosphorylation and activity of Mst1/2 and YAP/TAZ are regulated by phosphatases. The stability of Lats1/2 and YAP/TAZ is regulated by protein ubiquitination; LATS1/2 activity is also regulated by cytoskeleton. Despite extensive research on the hippo pathway in the past decade, the exact nature of the extracellular signals and membrane receptors that regulate the hippo pathway remains elusive.

## Cytoskeleton Regulation of Hippo Signaling Pathway



Cells in the body can feel the mechanical force generated by the neighbouring cells, extracellular matrix, the surrounding body fluids transmitted by the cells and the cell's own morphological changes, and adapt to the effects of mechanical force changes by regulating cell proliferation, differentiation, apoptosis or migration. As an important part of the cytoskeleton, microfilaments and microtubules play an important role in sensing and transducing mechanical force signals, and participate in the regulation of cell proliferation and differentiation. The latest research found that microfilaments in Drosophila and mammalian cells can regulate cell proliferation through the Hippo signaling pathway.

## In cancer

Many genes involved in the Hippo signaling pathway are considered tumor suppressors, while Yki/YAP/TAZ are identified as oncogenes. YAP/TAZ can reprogram cancer cells into cancer stem cells. YAP has been found to be elevated in certain human cancers, including breast cancer, colorectal cancer, and liver. In human cancer, many of the recognized components of the tumor suppressor gene pathway have undergone mutations. The role of components of the hippo pathway in cancer may be much more subtle than previously thought. The inactivation of the hippo pathway enhances the effects of 15 FDA-approved tumor drugs by promoting chemical retention.

**Featured Protein Products Related to NF-κB Signal Pathway**

Group	Cat.No.	Product Name	Tag	Species	Source
CD44	CD44-001H	Recombinant Human CD44 Protein, Myc/DDK-tagged	Myc/DDK	Human	HEK293T
	CD44-3095HA	Recombinant Human CD44 protein, Fc-tagged, APC labeled	Fc	Human	HEK293
	CD44-3095HP	Recombinant Human CD44 protein, Fc-tagged, R-PE labeled	Fc	Human	HEK293
	CD44-393H	Recombinant Human CD44 Protein (21-606 aa), His-SUMO-tagged	HisSUMO	Human	E.coli
	CD44-27238TH	Recombinant Human CD44 protein, GST-tagged	GST	Human	Wheat Germ
	CD44-3096H	Recombinant Human CD44 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
FAT4	CD44-3961H	Recombinant Human CD44 protein, His-tagged	His	Human	HEK293
	FAT4-5695M	Recombinant Mouse FAT4 Protein	His	Mouse	Mammalian Cell
TJP2	TJP2-3246H	Recombinant Human TJP2, His-tagged	His	Human	E.coli
AMOT	AMOT-528H	Recombinant Human AMOT protein, GST-tagged	GST	Human	Wheat Germ
YAP1	YAP1-1556H	Recombinant Human YAP1 Protein (1-504 aa), His-tagged	His	Human	Yeast
	YAP1-18H	Recombinant Human YAP1 protein, GST-tagged	GST	Human	Wheat Germ
	YAP1-19H	Recombinant Human YAP1 protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
TAZ	TAZ-1227H	Recombinant Human TAZ protein, His & T7-tagged	HisT7	Human	E.coli
	TAZ-30938TH	Recombinant Human TAZ	N/A	Human	Wheat Germ
FRMD1	FRMD1-4498H	Recombinant Human FRMD1 Protein, GST-tagged	GST	Human	Wheat Germ
FRMD3	FRMD3-4499H	Recombinant Human FRMD3 Protein, GST-tagged	GST	Human	Wheat Germ
FRMD4A	FRMD4A-6038M	Recombinant Mouse FRMD4A Protein	His	Mouse	Mammalian Cell
FRMD4B	FRMD4B-6039M	Recombinant Mouse FRMD4B Protein	His	Mouse	Mammalian Cell
FRMD5	FRMD5-4501H	Recombinant Human FRMD5 Protein, GST-tagged	GST	Human	Wheat Germ

Group	Cat.No.	Product Name	Tag	Species	Source
FRMD6	FRMD6-4502H	Recombinant Human FRMD6 Protein, GST-tagged	GST	Human	Wheat Germ
FRMD7	FRMD7-4503H	Recombinant Human FRMD7 Protein, GST-tagged	GST	Human	Wheat Germ
FRMD8	FRMD8-27032TH	Recombinant Human FRMD8, His-tagged	His	Human	E.coli
	FRMD8-4205H	Recombinant Human FRMD8 Protein, GST-tagged	GST	Human	Wheat Germ
WWC1	WWC1-5053H	Recombinant Human WWC1, His-tagged	His	Human	E.coli
NF2	NF2-22H	Recombinant Human NF2 protein, GST-tagged	GST	Human	Wheat Germ
	NF2-747H	Recombinant Human NF2 Protein, His-tagged	His	Human	E.coli
RASSF1	RASSF1-376H	Recombinant Human Ras association (RalGDS/AF-6) domain family member 1, His-tagged	His	Human	E.coli
	RASSF1-740H	Recombinant Human RASSF1	His	Human	Mammalian Cell
RASSF2	RASSF2-4942R	Recombinant Rat RASSF2 Protein	His	Rat	Mammalian Cell
	RASSF2-2575C	Recombinant Chicken RASSF2	His	Chicken	Mammalian Cell
RASSF3	RASSF3-2193H	Recombinant Human RASSF3, His-tagged	His	Human	E.coli
RASSF4	RASSF4-2194H	Recombinant Human RASSF4, GST-tagged	GST	Human	E.coli
RASSF5	RASSF5-1071H	Recombinant Human RASSF5, GST-tagged	GST	Human	E.coli
	RASSF5-29658TH	Recombinant Human RASSF5, His-tagged	His	Human	E.coli
	RASSF5-5443H	Recombinant Human RASSF5, MYC/DDK-tagged	Myc/DDK	Human	HEK293
RASSF6	RASSF6-2153H	Recombinant Human RASSF6 Protein (1-303 aa), GST-tagged	GST	Human	E.coli
RASSF7	RASSF7-2195H	Recombinant Human RASSF7, His-tagged	His	Human	E.coli
	RASSF7-664H	Recombinant Human RASSF7 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
RASSF8	RASSF8-493H	Recombinant Human RASSF8 Protein, GST-tagged	GST	Human	Wheat Germ

Group	Cat.No.	Product Name	Tag	Species	Source
RASSF9	RASSF9-13971M	Recombinant Mouse RASSF9 Protein	His	Mouse	Mammalian Cell
RASSF10	RASSF10-13963M	Recombinant Mouse RASSF10 Protein	His	Mouse	Mammalian Cell
SIK1	SIK1-432H	Recombinant Human SIK1 protein, His-tagged	His	Human	E.coli
	SIK1-48H	Recombinant Human SIK, GST-tagged	GST	Human	Sf9 Insect Cell
SIK2	SIK2-1954H	Recombinant Human SIK2 protein, His & T7-tagged	His T7	Human	E.coli
	SIK2-415H	Recombinant Human Salt-inducible Kinase 2, GST-tagged, Active	GST	Human	Sf9 Insect Cell
SIK3	SIK3-1482H	Recombinant Human SIK3 (Active), GST-tagged	GST	Human	Sf9 Insect Cell
PPP2R2C	PPP2R2C-2762H	Recombinant Human PPP2R2C Protein (1-447 aa), His-Myc-tagged	His Myc	Human	Insect Cell
	PPP2R2C-1917H	Recombinant Human PPP2R2C, GST-tagged	GST	Human	E.coli
	PPP2R2C-27932TH	Recombinant Human PPP2R2C	N/A	Human	Wheat Germ
STK11	STK11-23H	Recombinant Human STK11 protein, His-tagged	His	Human	E.coli
	STK11-240H	Recombinant Human STK11 protein, GST/His-tagged	GST His	Human	E.coli
MST1	MST1-2088H	Recombinant Human MST1 Protein, MYC/DDK-tagged	Myc DDK	Human	HEK293
	MST1-5670H	Recombinant Human MST1 Protein, GST-tagged	GST	Human	Wheat Germ
MARK4	MARK4-1058H	Recombinant Human MAP/Microtubule Affinity-Regulating Kinase 4, GST-tagged	GST	Human	Sf9 Insect Cell
	MARK4-29129TH	Recombinant Human MARK4	N/A	Human	Sf9 Insect Cell
SAV1	SAV1-14689M	Recombinant Mouse SAV1 Protein	His	Mouse	Mammalian Cell
	SAV1-4082R	Recombinant Rhesus monkey SAV1 Protein, His-tagged	His	Rhesus Macaque	Mammalian Cell
RHOB	RHOB-2291H	Recombinant Human RHOB, GST-tagged	GST	Human	E.coli
	RHOB-27380TH	Recombinant Human RHOB, His-tagged	His	Human	E.coli

Group	Cat.No.	Product Name	Tag	Species	Source
RHOA	RHOA-1182H	Recombinant Human RHOA Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
	RHOA-179H	Recombinant Human RHOA, His-tagged	His	Human	E.coli
	RHOA-2290H	Recombinant Human RHOA, GST-tagged	GST	Human	E.coli
	RHOA-27379TH	Recombinant Human RHOA	N/A	Human	E.coli
Rhod	Rhod-644M	Recombinant Mouse Rhod Protein, MYC/DDK-tagged	MYC/DDK	Mouse	HEK293T
	RHOD-2293H	Recombinant Human RHOD, His-tagged	His	Human	E.coli
RHOH	RHOH-2294H	Recombinant Human RHOH, GST-tagged	GST	Human	E.coli
RHOF	RHOF-1180H	Recombinant Human RHOF Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
RHOQ	RHOQ-1192H	Recombinant Human RHOQ protein, His & GST-tagged	His GST	Human	E.coli
	RHOQ-2296H	Recombinant Human RHOQ, His-tagged	His	Human	E.coli
MOB1A	MOB1A-396H	Recombinant Human MOB1A Protein, His-tagged	His	Human	E.coli
	MOB1A-5455H	Recombinant Human MOB1A Protein, GST-tagged	GST	Human	Wheat Germ
MOB1B	MOB1B-507H	Recombinant Human MOB1B, GST-tagged	His	Human	E.coli
	MOB1B-7582H	Recombinant Human MOB1B, His-tagged	His	Human	E.coli
ACTA2	ACTA2-7153H	Recombinant Human ACTA2 protein, His-tagged	His	Human	E.coli
	ACTA2-7155H	Recombinant Human ACTA2 protein, GST-tagged	GST	Human	E.coli
	ACTA2-189H	Recombinant Human ACTA2 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
AJUBA	AJUBA-581R	Recombinant Rat AJUBA Protein	His	Rat	Mammalian Cell
ITCH	ITCH-5004H	Recombinant Human ITCH Protein, GST-tagged	GST	Human	Wheat Germ
PP1	PP1-001R	Recombinant Rabbit PP1 Protein		Rabbit	E. coli
VGLL4	VGLL4-18014M	Recombinant Mouse VGLL4 Protein	His	Mouse	Mammalian Cell

Group	Cat.No.	Product Name	Tag	Species	Source
	VGLL4-5156R	Recombinant Rhesus monkey VGLL4 Protein, His-tagged	His	Rhesus Macaque	Mammalian Cell
TEAD1	TEAD1-1381H	Recombinant Human TEAD1 Protein, His-tagged	His	Human	Yeast
	TEAD1-3174H	Recombinant Human TEAD1, GST-tagged	GST	Human	E.coli
TEAD2	TEAD2-26H	Recombinant Human TEAD2 protein, GST-tagged	GST	Human	Wheat Germ
	TEAD2-33H	Recombinant Human TEAD2 protein, His-tagged	His	Human	E.coli
	TEAD2-34H	Recombinant Human TEAD2 protein, His/Sumo-tagged	His SUMO	Human	E.coli
TEAD3	TEAD3-1382H	Recombinant Human TEAD3 Protein, His-SUMO-tagged	His SUMO	Human	E.coli
	TEAD3-27H	Recombinant Human TEAD3 protein, GST-tagged	GST	Human	Wheat Germ
TEAD4	TEAD4-1005H	Recombinant Human TEAD4 Protein (74-434 aa), His-SUMO-tagged	His SUMO	Human	E.coli
	TEAD4-3175H	Recombinant Human TEAD4, GST-tagged	GST	Human	E.coli
SMAD1	SMAD1-11H	Recombinant Human SMAD1, His-tagged	His	Human	E.coli
	SMAD1-12H	Recombinant Human SMAD1, MYC/DDK-tagged	Myc DDK	Human	HEK293
	SMAD1-161H	Recombinant Human SMAD1 Protein, His-tagged	His	Human	E.coli
SMAD2	SMAD2-118H	Recombinant Human SMAD2 protein, T7/His-tagged	T7 His	Human	E.coli
	SMAD2-1915H	Recombinant Human SMAD2 Protein, MYC/DDK-tagged	Myc DDK	Human	HEK293
	SMAD2-294H	Recombinant Human SMAD2 protein, GST-tagged	GST	Human	E.coli
	SMAD2-30446TH	Recombinant Human SMAD2, His-tagged	His	Human	E.coli
	SMAD2-324H	Recombinant Human SMAD2 protein, His/MBP-tagged	His MBP	Human	E.coli
SMAD3	SMAD3-1918H	Recombinant Human SMAD3 Protein, MYC/DDK-tagged	Myc DDK	Human	HEK293
	SMAD3-295H	Recombinant Human SMAD3 protein, GST-tagged	GST	Human	E.coli
	SMAD3-304H	Recombinant Human SMAD3 Protein, His-tagged	His	Human	E.coli

Group	Cat.No.	Product Name	Tag	Species	Source
SMAD4	SMAD4-1095H	Recombinant Human SMAD Family Member 4, GST-tagged	GST	Human	E.coli
	SMAD4-217H	Recombinant Human SMAD4 protein, His-tagged	His	Human	E.coli
SMAD5	SMAD5-162H	Recombinant Human SMAD5 Protein, His-tagged	His	Human	E.coli
	SMAD5-2800H	Recombinant Human SMAD5, GST-tagged	GST	Human	E.coli
SMAD6	PGC-299H	Recombinant Human SMAD6 Protein, His-tagged	His	Human	E.coli
	SMAD6-1913H	Recombinant Human SMAD6 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
	SMAD6-22H	Recombinant Human SMAD6 Protein, GST-tagged	GST	Human	Wheat Germ
SMAD7	SMAD7-1912H	Recombinant Human SMAD7 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
	SMAD7-29105TH	Recombinant Human SMAD7	N/A	Human	Wheat Germ
SMAD9	SMAD9-1914H	Recombinant Human SMAD9 Protein, MYC/DDK-tagged	Myc/DDK	Human	HEK293
	SMAD9-234H	Recombinant Human SMAD9, GST-tagged	GST	Human	E.coli
	SMAD9-302H	Recombinant Human SMAD9 Protein, His/GST-tagged	His/GST	Human	E.coli
TP73	TP73-30579TH	Recombinant Human TP73	N/A	Human	Sf9 Insect Cell
	TP73-328H	Recombinant Human Tumor Protein P73, GST-tagged	GST	Human	Sf9 Insect Cell

