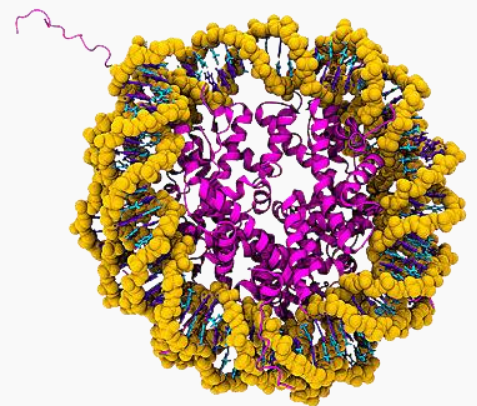


# The p53 Pathway

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## The p53 Pathway

The p53 pathway is composed of a network of genes and their products that are targeted to respond to a variety of intrinsic and extrinsic stress signals, which impact cellular homeostatic mechanisms that monitor DNA replication, chromosome segregation, and cell division (Vogelstein et al., 2000). The p53 pathway responds to stresses that can disrupt the fidelity of DNA replication and cell division. Mechanistically, a stress signal is transmitted to the p53 protein by post-translational modifications, which activates the p53 protein as a transcription factor that initiates a program of cell cycle arrest, cellular senescence, or apoptosis. The transcriptional network of p53-responsive genes produces proteins that interact with many other signal transduction pathways in the cell, and a number of positive and negative auto-regulatory feedback loops act upon the p53 response. To further elaborate, the p53 circuit communicates with the Wnt-beta-catenin, IGF-1-AKT, Rb-E2F, p38 MAP kinase, cyclin-CDK, p14/19 ARF pathways, and the cyclin G-PP2A and p73 gene products.

### p53

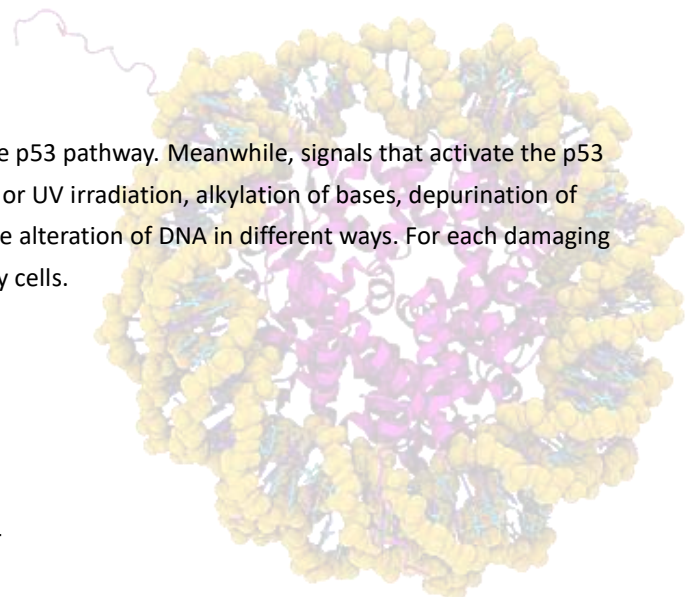
p53 is an important tumor suppressor gene. Since the discovery of the p53 gene in 1979, over 80,000 research papers have been reported. Initially, the p53 gene was thought to be an oncogene, but with the deepening of research during the past decades, the function of p53 as a tumor suppressor was gradually revealed. Furthermore, mutations in the p53 gene have been found in more than 50% of human tumor tissues, which is the most common genetic modification in tumors, indicating that the p53 gene is likely to be the major pathogenic factor of tumors.

After the discovery of the p53 gene in humans, monkeys, chickens, and mice, it was mapped. The human p53 gene was located on 17p13, the mouse p53 was located on chromosome 11 and a nonfunctional pseudogene was found on chromosome 14. Among animals with different degrees of evolution, p53 has a very similar gene structure, about 20 KB long, composed of 11 exons and 10 introns. The first exon is non-coded, and exon-2, -4, -5, -7, and -8 encode five evolutionarily highly conserved domains and five highly conserved regions of the p53 gene, namely the 13-19, 117-142, 171-192, 236-258, and 270-286 coding regions. The p53 gene is further transcribed into a 2.5 kb mRNA, encoding 393 amino acid proteins with a molecular weight of 43.7 kDa. The expression of the p53 gene is regulated at least at the transcriptional and post-transcriptional levels.

Human p53 is active as a homotetramer of  $4 \times 393$  amino acids with a complex domain organization, consisting of an intrinsically disordered N-terminal transactivation domain (TAD), a proline (Pro)-rich region, a structured DNA-binding domain (DBD), and tetramerization domain connected via a flexible linker, and an intrinsically disordered C-terminal regulatory domain. The p53 tetramers have a dimer-of-dimers topology, and individual subunits within the human tetramerization domain (residues 325–355) are composed of a short  $\beta$ -strand followed by a sharp turn leading into an  $\alpha$  helix.

### The p53 pathway activation

Stresses, both intrinsic and extrinsic to the cell, can act upon the p53 pathway. Meanwhile, signals that activate the p53 protein can damage the integrity of the DNA template. Gamma or UV irradiation, alkylation of bases, depurination of DNA, or reaction with oxidative free radicals all contribute to the alteration of DNA in different ways. For each damaging agent, a unique detection and repair mechanism is employed by cells.



Different types of DNA damage appear to activate unique enzyme activities that modify the p53 protein at particular amino-acid residues. As a result, the nature of the stress signal is transmitted to the protein, presumably its activity, by a code inherent to the post-translational modifications that reflect the different types of stress. For example, gamma-radiation activates the ATM kinase and the CHK-2 kinase, which can phosphorylate the p53 protein, while UV-radiation activates ATR, CHK-1, and casein kinase-2, which results in the modification of different amino-acid residues on the p53 protein (Appella and Anderson, 2001). For most of these stress signals, the p53 protein is modified by phosphorylation and acetylation, which appear to alter the p53 protein in two ways: First, the half-life of the protein in a cell increases from 6–20 min to hours, resulting in a 3–10-fold increased concentration of the p53 protein in a cell; Second, enhanced ability of the p53 protein to bind to specific DNA sequences and promotion of gene transcription regulated by DNA sequences.

The activation of the p53 protein in response to stresses is mediated and regulated by protein kinases, histone acetyltransferases, methylases, ubiquitin, and sumo ligases. As the p53 protein is activated by these protein modifications, it can also be inactivated by phosphatases, histone deacetylases, ubiquitinates, or even inhibitors of ubiquitin ligases. In addition, the activated p53 protein interacts with many important proteins for its transcriptional activity, such as PML bodies (promyelocytic leukemia bodies) and the Werner helicase. Several of these associated proteins are essential for p53 transcriptional activities or even the selective modulation of genes that p53 may regulate in its pathway to carry out its functions.

### Downstream events of the p53 pathway

Once the p53 protein is activated, it initiates a transcriptional program. The activated p53 protein binds to a specific DNA sequence, termed the p53-responsive element (RE), composed of RRRCWGYYY (spacer of 0–21 nucleotides), where R is a purine, W is A or T, and Y is a pyrimidine. Thus, two degenerate 10 bp sequences separated in the genome by a variable length spacer are required to regulate the p53-responsive genes. Genes in this p53 network initiate one of three programs that result in cell cycle arrest (G-1 or G-2 blocks are observed), cellular senescence, or apoptosis.

#### 1. Cell-cycle arrest

Cell-cycle arrest by p53 is mainly mediated by the transcriptional activation of p21/WAF1. p53 can activate the transcriptional upregulation of CDKN1A, which encodes for cell cycle inhibitor p21. The p21 mRNA is highly induced after p53 activation and is the first p53 target gene. p21 binds to cyclin E/Cdk2 and cyclin D/Cdk4 complexes to cause G1 arrest in the cell cycle (Harper et al. 1993). The inhibition of Cdk2 and Cdk4 by p21 blocks pRb phosphorylation, promotes pRb binding to E2F1, and promotes transcription silencing of E2F1 targets critical for DNA replication and cell-cycle progression.

In addition, p53 activation also arrests cells at the G2/M phases. Although p21 can also inhibit cyclin B/Cdc2 from inhibiting cell-cycle progression through mitosis, other p53 target genes, such as 14-3-3 $\sigma$ , may participate in blocking the G2/M transition.

#### 2. Cellular senescence

Cellular senescence is defined as a cell state characterized by prolonged and generally irreversible cell-cycle arrest and the acquisition of different phenotypic alterations, including morphological changes, chromatin remodeling, metabolic reprogramming, and secretion of pro-inflammatory factors or SASP (senescence-associated secretory phenotypes).

Cellular senescence mediates via p53-induced transcriptional activation of the cyclin-dependent kinase (CDK) inhibitors P21CIP1 (CDKN1A) and P16 INK4A (CDKN2A). The role of P21CIP1 may be to initiate senescence, whereas P16INK4A may be responsible for durable growth arrest. Apart from P21INK4A, there are other target genes like PML nuclear body scaffold (PML) and SERPINE1 (Serpin family E member 1), also known as Plasminogen activator inhibitor-1 (PAI-1), which are transcriptionally activated by p53 and plays a role in senescence.

### 3. Apoptosis

Many apoptosis-related genes transcriptionally regulated by p53 have been identified, which are candidates for implementing p53 effector functions. In response to oncogene activation, p53 mediates apoptosis through a linear pathway involving Bax transactivation, Bax translocation from the cytosol to membranes, cytochrome c release from mitochondria, and caspase-9 activation, followed by the activation of caspase-3, -6, and -7. p53-mediated apoptosis can be blocked at multiple death checkpoints by inhibiting p53 activity directly, by Bcl-2 family members regulating mitochondrial function, by E1B 19K blocking caspase-9 activation, and by caspase inhibitors.

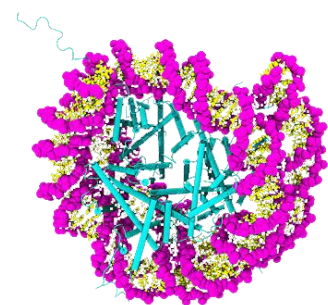
### p53 cancer mutations

In over 50% of human cancer types, p53 is directly inactivated by mutation. The prevalence of p53 mutation varies significantly by cancer type and also depends on the developmental stage of a tumor, ranging from less than 5% in cervical cancer and 10% in leukemia to 80% in small-cell lung cancer and 90% in ovarian cancer. Most cancer-associated mutations are located in the DBD, which involves several mutational hotspots, with the most frequent somatic cancer mutations being R175H, Y220C, G245S, R248Q/W, R249S, R273C/H, and R282W.

### p53 in cancer therapy

Dysfunction of the p53 gene occurs in most, if not all, human malignancies. Two principal mechanisms are responsible for this dysfunction: mutation and down-regulation of wild-type p53 mediated by MDM2/MDM4. Because of its almost universal inactivation in malignancy, p53 is a highly attractive target for the development of new anticancer drugs. There have been at least seven different approaches to developing translational therapies for the p53 protein and pathway.

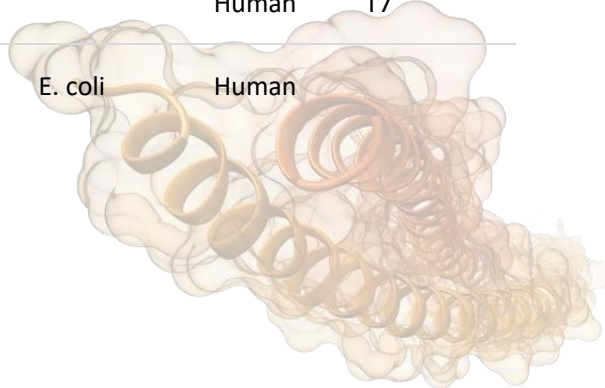
- Small-Molecule Stabilizers of p53 – the Y220C Paradigm
- Rescue of Zinc-Binding – Deficient Mutants with Metallochaperones
- Alkylating Agents and DNA Intercalators
- Rescue of Nonsense Mutated p53
- Targeting the Tetramerization Domain
- Inhibitors of the p53 – MDM2/MDMX Interaction
- Targeting Other p53 Modulators



Despite nearly 40 years of research on p53, resulting in a staggering 80,000 publications, there are only beginning to grasp the full complexity of the p53 pathway, and the future will undoubtedly bring many novels, sometimes surprising, or even paradigm-shifting discoveries. Nevertheless, Creative BioMart is ready to provide a list of related protein products to support your ongoing research. Please feel free to contact us if you're interested.

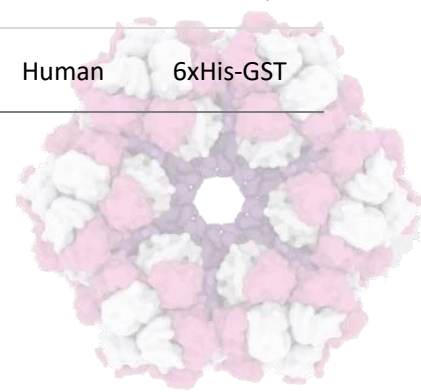


Group	Cat.No.	Product Name	Source	Species	Tag
PRKAB1	PRKAB1-347H	Recombinant Human protein kinase, AMP-activated, beta 1 non-catalytic subunit, His-tagged	E.coli	Human	His-tag
	PRKAB1-1945H	Recombinant Human PRKAB1, His-tagged	E.coli	Human	His
	PRKAB1-3081H	Recombinant Human PRKAB1 protein, His-tagged	E. coli	Human	His
	PRKAB1-3249H	Recombinant Human PRKAB1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	PRKAB1-1785H	Recombinant Human PRKAB1 protein, His & GST-tagged	E. coli	Human	His & GST
	PRKAB1-370H	Recombinant Human PRKAB1 protein, His/MBP-tagged	E. coli	Human	His/MBP
PRKAB2	PRKAB2-368H	Recombinant Human PRKAB2 protein, His/MBP-tagged	E. coli	Human	His/MBP
	PRKAB2-237H	Recombinant Human PRKAB2 protein, His-tagged	E. coli	Human	His
	PRKAB2-1946H	Recombinant Human PRKAB2, GST-tagged	E.coli	Human	GST
	PRKAB2-378H	Recombinant Human protein kinase, AMP-activated, beta 2 non-catalytic subunit, His-tagged	E.coli	Human	His-tag
TSC1	TSC1-494H	Recombinant Human TSC1 Protein, His-tagged	E. coli	Human	N-His
TSC2	TSC2-35H	Recombinant Human TSC2 protein, His-tagged	E. coli	Human	His
RHEB	RHEB-5588H	Recombinant Human RHEB Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	RHEB-1181H	Recombinant Human RHEB Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	RHEB-521H	Recombinant Human RHEB, His tagged	Baculovirus-Insect cells	Human	His
	RHEB-2289H	Recombinant Human RHEB, His-tagged	E.coli	Human	His
	RHEB-31325TH	Recombinant Human RHEB, T7 -tagged		Human	T7
	RHEB-31326TH	Recombinant Human RHEB	E. coli	Human	



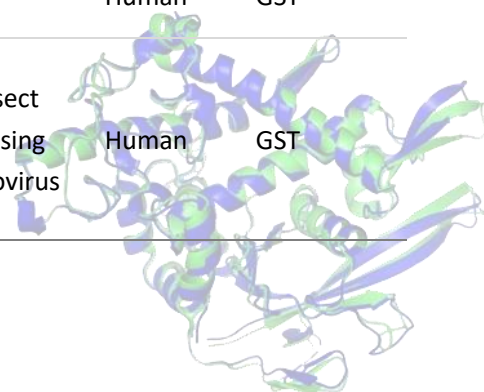


PTEN	PTEN-1619H	Recombinant Human Phosphatase And Tensin Homolog, GST-tagged		Human	
	PTEN-2042H	Recombinant Human PTEN, GST-tagged	E.coli	Human	GST
	PTEN-342H	Recombinant Human PTEN Protein, His-tagged	E. coli	Human	His
	PTEN-31H	Recombinant Human PTEN Protein, His-tagged	Insect cells	Human	His
	PTEN-2403H	Recombinant Human PTEN Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	PTEN-663H	Recombinant Human PTEN Protein, His-tagged	Sf9 cells	Human	His
AKT1	AKT1-1363H	Recombinant Human AKT1 (Active), GST-tagged	Sf9 Cells	Human	GST
	AKT1-56H	Recombinant Human AKT1, Activated	Sf9 insect cells.		
	AKT1-14H	Recombinant Human AKT1 Protein, His-tagged	Insect cells	Human	His
	AKT1-259H	Recombinant Human AKT1 protein, His-tagged	Insect cells	Human	His
	AKT1-50H	Recombinant Human AKT1 protein, GST-tagged	Insect cells	Human	GST
	AKT1-47H	Recombinant Human AKT1 protein, His-tagged	E. coli	Human	His
	AKT1-3920H	Recombinant Human AKT1 protein, GST-tagged	E. coli	Human	GST
	AKT1-307H	Recombinant Human AKT1 protein, His/MBP-tagged	E. coli	Human	His/MBP
	AKT1-30H	Recombinant Human AKT1 protein, Flag-tagged, Biotinylated	Insect cell	Human	Flag
	AKT1-155H	Recombinant Human AKT1 protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	AKT1-1516H	Recombinant Human AKT1 protein	E. coli	Human	
	AKT1-420H	Recombinant Human AKT1 Protein, GST-His tagged	Insect Cell	Human	GST-His
	AKT1-336H	Recombinant Human AKT1 protein, His/Strep-tagged	HEK293	Human	His/Strep
	AKT1-001H	Recombinant Human AKT1 Protein, His-GST-tagged	E. coli	Human	6xHis-GST



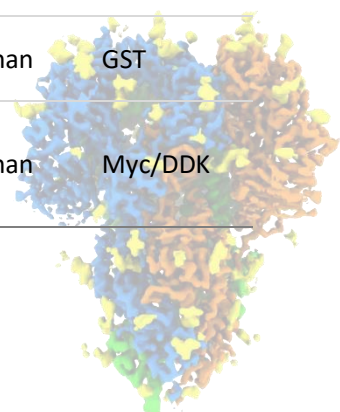


	AKT1-014H	Recombinant Human AKT1 Protein, MYC/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	AKT1-5186H	Recombinant Human AKT1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	AKT1-2503H	Recombinant Human AKT1 protein, GST-tagged	E. coli	Human	GST
	AKT1-2689H	Recombinant Human AKT1 protein, His-tagged	E. coli	Human	His
	AKT1-786HF	Recombinant Human AKT1 Protein, His-tagged, FITC conjugated	Insect cells	Human	His
	AKT1-786HAF488	Recombinant Human AKT1 Protein, His-tagged, Alexa Fluor 488 conjugated	Insect cells	Human	His
	AKT1-786HAF555	Recombinant Human AKT1 Protein, His-tagged, Alexa Fluor 555 conjugated	Insect cells	Human	His
	AKT1-786HAF647	Recombinant Human AKT1 Protein, His-tagged, Alexa Fluor 647 conjugated	Insect cells	Human	His
AKT2	AKT2-2504H	Recombinant Human AKT2 protein, His-SUMO-tagged	E. coli	Human	His-SUMO
	AKT2-31H	Recombinant Human AKT2 protein, Flag-tagged, Biotinylated	Insect cell	Human	Flag
	AKT2-1841H	Recombinant Human AKT2 protein, His & T7-tagged	E. coli	Human	His & T7
	AKT2-424H	Recombinant Human AKT2 Protein, GST-His tagged	Insect Cell	Human	GST-His
	AKT2-248H	Recombinant Human AKT2 Protein, His & GST-tagged	Baculovirus-Insect Cells	Human	His & GST
	AKT2-802H	Recombinant Human AKT2, GST-tagged	Sf9 cells	Human	GST
	AKT2-1364H	Recombinant Human AKT2 (Active), His-tagged	Sf9 Cells	Human	His
AKT3	AKT3-1365H	Recombinant Human AKT3 (Active), GST-tagged	Sf9 Cells	Human	GST
	AKT3-26H	Recombinant Human AKT3 (E17K), GST-tagged	Sf9 insect cells using baculovirus	Human	GST



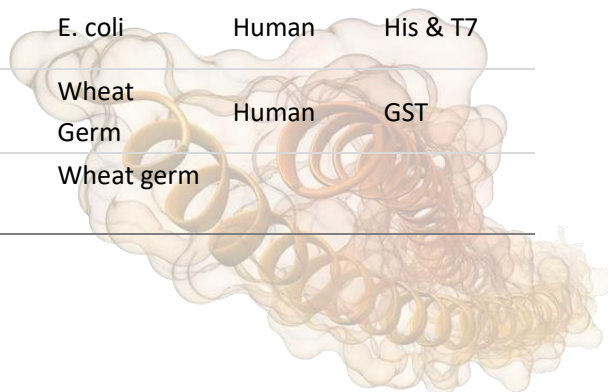


	AKT3-2522H	Recombinant Human AKT3, Active	E. coli.		
	AKT3-131H	Recombinant Human AKT3, GST-tagged	Baculovirus-Insect Cells	Human	GST
	Akt3-162H	Recombinant Human Akt3, GST-tagged	E. coli.	Human	GST
	AKT3-804H	Recombinant Human AKT3 protein, GST-His-tagged	Insect cells	Human	GST/His
	AKT3-104H	Recombinant Human AKT3, GST-tagged, Active	Sf9 insect cells using baculovirus	Human	GST
	AKT3-166H	Recombinant Human AKT3, His-tagged	E. coli	Human	
	AKT3-308H	Recombinant Human AKT3 protein, His/MBP-tagged	E. coli	Human	His/MBP
	AKT3-427H	Recombinant Human AKT3 Protein, GST-tagged	Wheat Germ	Human	GST
	AKT3-426H	Recombinant Human AKT3 Protein	Insect Cell	Human	
	AKT3-550H	Recombinant Human AKT3 Protein, His-tagged	E. coli	Human	His
	AKT3-1566H	Recombinant Human AKT3 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	AKT3-01H	Recombinant Human AKT3 Protein, His-tagged	HEK293	Human	His
BAD	BAD-26296TH	Recombinant Human BAD	E. coli		
	BAD-6973H	Recombinant Human BAD, GST-tagged	Sf9 Cells	Human	GST
	BAD-048H	Recombinant Human BAD protein, GST-tagged	Wheat Germ	Human	GST
	BAD-564H	Recombinant Human BAD Protein, His-tagged	E. coli	Human	His
CASP9	CASP9-618H	Recombinant Human CASP9	E. coli.		
	CASP9-0433H	Recombinant Human CASP9 Protein, GST-Tagged	Wheat Germ	Human	GST
	CASP9-3270H	Recombinant Human CASP9 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK

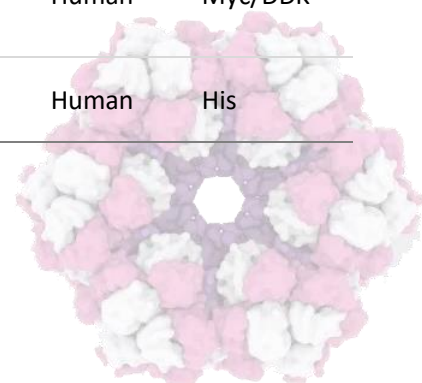




	CASP9-48H	Recombinant Human CASP9 protein, MYC/DDK-tagged	HEK293 cells	Human	MYC/DDK
	CASP9-49H	Recombinant Human CASP9 protein	E. coli	Human	
	CASP9-148H	Recombinant Human CASP9 Protein, His-tagged	E. coli	Human	His
	CASP9-626H	Recombinant Human CASP9 protein, His-tagged	E. coli	Human	His
	CASP9-627H	Recombinant Human CASP9 protein, His-tagged	E. coli	Human	His
	BAX-8493H	Recombinant human BAX protein, GST-tagged	E.coli	Human	GST
	BAX-3974H	Recombinant Human BAX Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	BAX-6977H	Recombinant Human BAX protein, His-tagged	E. coli	Human	His
	BAX-094H	Recombinant Human BAX Protein, GST-tagged	Wheat Germ	Human	GST
	BAX-095H	Recombinant Human BAX Protein, GST-tagged	Wheat Germ	Human	GST
BAX	BAX-26650TH	Recombinant Human BAX protein, GST-tagged	E. coli	Human	GST
	BAX-458H	Recombinant Human BAX	Mammalian Cells	Human	His
	BAX-6976H	Recombinant Human BAX, His-tagged	E. coli	Human	His
	BAX-6975H	Recombinant Human BAX, GST-tagged	E. coli	Human	GST
	BAX-31H	Recombinant Human BAX Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
	BAX-2780H	Recombinant Human BAX Protein, His-tagged, OVA Conjugated	Protein Conjugation	Human	N-His
	APAF1-018H	Recombinant Human APAF1 protein, His-B2M-tagged	E. coli	Human	His-B2M
	APAF1-1329H	Recombinant Human APAF1 Protein (104-415 aa), His-tagged	Yeast	Human	His
APAF1	APAF1-1442H	Recombinant Human APAF1 protein, His & T7-tagged	E. coli	Human	His & T7
	APAF1-665H	Recombinant Human APAF1 protein, GST-tagged	Wheat Germ	Human	GST
	APAF1-27358TH	Recombinant Human APAF1	Wheat germ		

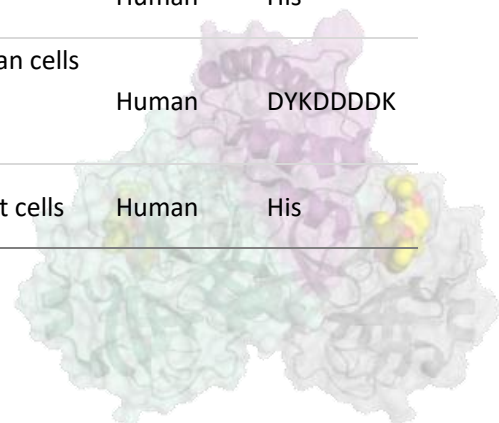


CASP3	CASP3-334H	Recombinant Human CASP3 protein, GST-tagged	Wheat Germ	Human	GST
	CASP3-293H	Recombinant Human CASP3 protein, His/MBP-tagged	E. coli	Human	His/MBP
	CASP3-621H	Recombinant Human CASP3 protein, His-tagged	E. coli	Human	His
	CASP3-622H	Recombinant Human CASP3 protein, His & T7-tagged	E. coli	Human	His & T7
	CASP3-188H	Recombinant Human CASP3 Protein, MYC/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CASP3-1333H	Recombinant Human CASP3 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CASP3-01H	Recombinant Human CASP3 Protein, His-tagged	E. coli	Human	His
	CASP3-0421H	Recombinant Human CASP3 Protein, GST-Tagged	Wheat Germ	Human	GST
	CASP3-1642H	Recombinant Human Caspase 3, Apoptosis-related Cysteine Peptidase	E. coli	Human	
	CASP3-192H	Recombinant Human CASP3, Met&His-tagged	E. coli	Human	&His
USP2	CASP3-625H	Recombinant Human CASP3 Protein, His-tagged	E. coli	Human	N-His
	CASP3-624H	Recombinant Human CASP3 Protein, His-tagged	E. coli	Human	N-His
	USP2-3620H	Recombinant Human USP2, GST-tagged	E.coli	Human	GST
	USP2-544H	Recombinant Human USP2 Protein, His-tagged	E. coli	Human	His
	USP2-1042H	Recombinant Human USP2	E. coli	Human	
	USP2-320H	Recombinant human USP2 protein, FLAG-tagged	Sf9 cell	Human	FLAG
	USP2-011H	Recombinant Human USP2 Protein, His-tagged	E. coli	Human	His
	USP2-886H	Recombinant Human USP2 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
USP2-092H	Recombinant Human USP2 Protein, His-tagged	E. coli	Human	His	

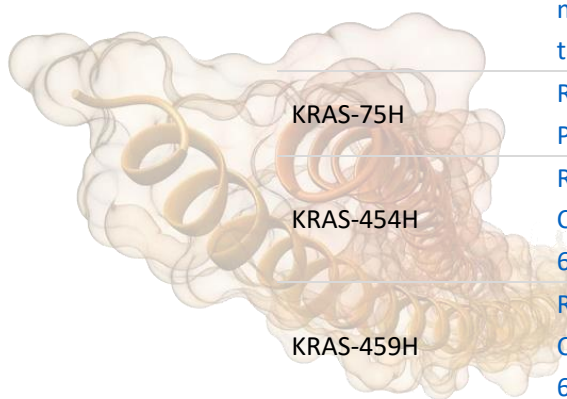




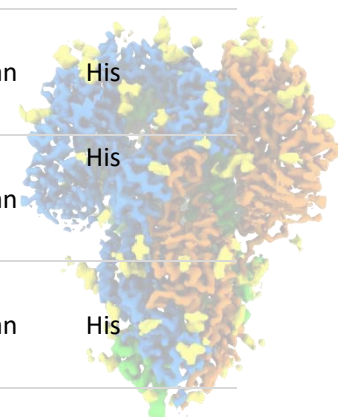
USP4	USP4-1915H	Recombinant Human USP4 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	USP4-359H	Recombinant Human USP4 Protein, GST-tagged	Bacteria	Human	GST
	USP4-42H	Recombinant Human USP4 protein, His-tagged	Insect cells	Human	His
	USP4-156H	Recombinant Human USP4	Insect Cells	Human	
	USP4-183H	Recombinant Human USP4, His-tagged	E. coli	Human	His
MDM2	MDM2-2319H	Recombinant Human MDM2	E. coli	Human	
	MDM2-6982H	Recombinant Human MDM2, GST-tagged	E. coli	Human	GST
	MDM2-1065H	Recombinant Human MDM2, GST-tagged	Wheat germ	Human	GST
	MDM2-105H	Recombinant Human MDM2, His-tagged	E. coli	Human	His
	MDM2-2320H	Recombinant Human MDM2, GST-tagged	E. coli	Human	GST
	MDM2-350H	Recombinant human MDM2, His-tagged	E.coli	Human	His
	MDM2-110H	Recombinant Human MDM2, His6-HA-SUMO-tagged	E.coli	Human	His6-HA-SUMO
	MDM2-1518H	Recombinant Human MDM2 protein	E. coli	Human	
	MDM2-134H	Recombinant Human MDM2 protein, T7/His-tagged	E. coli	Human	T7/His
MDM2-568H	Recombinant Human MDM2 Protein, His-tagged	E. coli	Human	His	
KRAS	KRAS-02H	Recombinant Human KRAS (G12D) Protein, His-tagged	E. coli	Human	His
	KRAS-078H	Recombinant Human KRAS G13D mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
	KRAS-451H	Recombinant Human KRAS(Met1-Lys169) Protein, N-6*His-tagged	E.coli	Human	His
	KRAS-01H	Recombinant Human KRAS G12D mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
	KRAS-19H	Recombinant Human KRAS protein, His-tagged	Insect cells	Human	His



KRAS-079H	Recombinant Human KRAS G12V mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-080H	Recombinant Human KRAS G12S mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-452H	Recombinant Human KRAS(Met1-Lys169) Protein, N-6*His-tagged	E.coli	Human	His
KRAS-085H	Recombinant Human KRAS Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-084H	Recombinant Human KRAS Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-083H	Recombinant Human KRAS G12A mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-082H	Recombinant Human KRAS G12C mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-081H	Recombinant Human KRAS G12D mutant Protein, DYKDDDDK-tagged	Human cells	Human	DYKDDDDK
KRAS-75H	Recombinant Human KRAS Protein, GST-tagged	E.coli	Human	GST
KRAS-454H	Recombinant Human KRAS(Thr2-Cys185(Gly12Val)) Protein, N-6*His-tagged	E.coli	Human	His
KRAS-459H	Recombinant Human KRAS(Thr2-Cys185(Gly12 Ser)) Protein, N-6*His-tagged	E.coli	Human	His
KRAS-450H	Recombinant Human KRAS(Met1-Lys169(Gly12Cys)) Protein, N-6*His-tagged	E.coli	Human	His
KRAS-4888H	Recombinant Human KRAS Protein, GST-tagged	Wheat Germ	Human	GST
KRAS-358H	Recombinant Human KRAS Protein, His-tagged	E. coli	Human	His
KRAS-3489H	Recombinant Human KRAS Protein, His-tagged	E. coli	Human	His
KRAS-031H	Recombinant Human KRAS Protein, MYC/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
KRAS-457H	Recombinant Human KRAS protein(G12C, Q61H), His-tagged	E. coli	Human	His



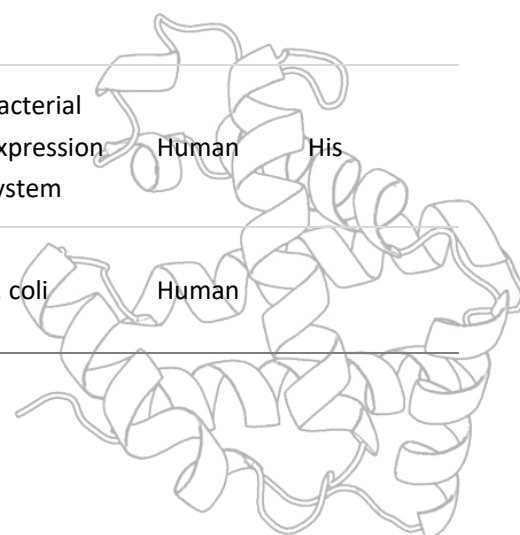
KRAS-458H	Recombinant Human KRAS protein(G12D, Q61H), His-tagged	E. coli	Human	His
KRAS-455H	Recombinant Human KRAS Protein, His-tagged	E. coli	Human	His
KRAS-163H	Recombinant Human KRAS protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
KRAS-456H	Recombinant Human KRAS Protein, His-tagged	E. coli	Human	His
KRAS-547H	Recombinant Human Kirsten rat sarcoma viral oncogene homolog, His-tagged	E.coli	Human	His-tag
KRAS-1246H	Recombinant Human V-Ki-ras2 Kirsten Rat Sarcoma Viral Oncogene Homolog	E. coli	Human	
KRAS-325H	Recombinant Human KRAS, His-tagged	E. coli	Human	His
KRAS-03H	Recombinant Human KRAS Protein, DYKDDDDK-tagged	Human Cells	Human	DYKDDDDK
KRAS-04H	Recombinant Human KRAS Protein, Myc/DDK-tagged	HEK293	Human	Myc/DDK
KRAS-10H	Recombinant Human KRAS (G12C) Mutant Protein, His-tagged	E. coli	Human	His
KRAS-3965HAF555	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 555 conjugated	E. coli	Human	His
KRAS-455HAF555	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 555 conjugated	E. coli	Human	His
KRAS-456HAF555	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 555 conjugated	E. coli	Human	His
KRAS-3965HAF647	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 647 conjugated	E. coli	Human	His
KRAS-455HAF647	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 647 conjugated	E. coli	Human	His
KRAS-456HAF647	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 647 conjugated	E. coli	Human	His
KRAS-3965HF	Recombinant Human KRAS Protein, His-tagged, FITC conjugated	E. coli	Human	His







	KRAS-455HF	Recombinant Human KRAS Protein, His-tagged, FITC conjugated	E. coli	Human	His
	KRAS-456HF	Recombinant Human KRAS Protein, His-tagged, FITC conjugated	E. coli	Human	His
	KRAS-3965HAF488	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 488 conjugated	E. coli	Human	His
	KRAS-455HAF488	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 488 conjugated	E. coli	Human	His
	KRAS-456HAF488	Recombinant Human KRAS Protein, His-tagged, Alexa Fluor 488 conjugated	E. coli	Human	His
ERAS	ERAS-1972H	Recombinant Human ERAS Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ERAS-1261H	Recombinant Human ERAS Protein (3-230 aa), His-tagged	E. coli	Human	His
	ERAS-3440H	Recombinant Human ERAS Protein, GST-tagged	Wheat Germ	Human	GST
MRAS	MRAS-703H	Recombinant Human MRAS (Q71L) Protein, His-tagged	E. coli	Human	His
	MRAS-5533H	Recombinant Human MRAS Protein, GST-tagged	Wheat Germ	Human	GST
	MRAS-2960H	Recombinant Human MRAS Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	MRAS-1104H	Recombinant Human MRAS Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	MRAS-885H	Recombinant Human MRAS	Mammalian Cells	Human	His
	MRAS-1335H	Recombinant Human Muscle RAS Oncogene Homolog, His-tagged			
NRAS	NRAS-01H	Recombinant Human NRAS Protein, His-tagged	Bacterial expression system	Human	His
	NRAS-1279H	Recombinant Human Neuroblastoma RAS Viral (v-ras) Oncogene Homolog	E. coli	Human	

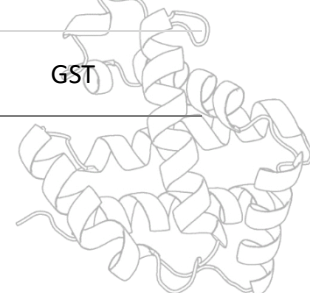


	NRAS-30411TH	Recombinant Human NRAS Protein	E. coli	Human	
	NRAS-165H	Recombinant Human NRAS protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	NRAS-447H	Recombinant Human NRAS Protein, His-tagged	E. coli	Human	His
	NRAS-4434H	Recombinant Human NRAS protein, 10xHis-GST&Myc-tagged	E. coli	Human	His-GST&Myc
	NRAS-3519H	Recombinant Human NRAS Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	NRAS-6106H	Recombinant Human NRAS Protein, GST-tagged	Wheat Germ	Human	GST
CCND1	CCND1-23H	Recombinant Human CCND1 protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	CCND1-221H	Recombinant Human CCND1 protein, T7/His-tagged	E. coli	Human	T7/His
	CCND1-171H	Recombinant Human CCND1 protein, DDK-tagged	Insect cells	Human	DDK
	CCND1-354H	Recombinant Human CCND1 protein, His/MBP-tagged	E. coli	Human	His/MBP
	CCND1-355H	Recombinant Human CCND1 protein, His/MBP-tagged	E. coli	Human	His/MBP
	CCND1-834H	Recombinant Human CCND1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CCND1-21H	Recombinant Human CCND1 protein, His-tagged	E. coli	Human	His
	CCND1-3456H	Recombinant Human CCND1 protein, His-tagged	E. coli	Human	His
	CCND1-24H	Recombinant Human CCND1 protein, Flag-tagged	Insect cells	Human	Flag
	CCND1-483H	Recombinant Human CCND1 Protein, His-GST-tagged	E. coli	Human	His-GST
	CCND1-0658H	Recombinant Human CCND1 Protein, GST-Tagged	Wheat Germ	Human	GST
	IGLC1-14119H	Recombinant Human IGLC1, His-tagged	E.coli	Human	His
	CCND1-27756TH	Recombinant Human CCND1	E. coli	Human	
	CCND2	CCND2-10861H	Recombinant Human CCND2, GST-tagged	E.coli	Human
CCND2-0659H		Recombinant Human CCND2 Protein, GST-Tagged	Wheat Germ	Human	GST

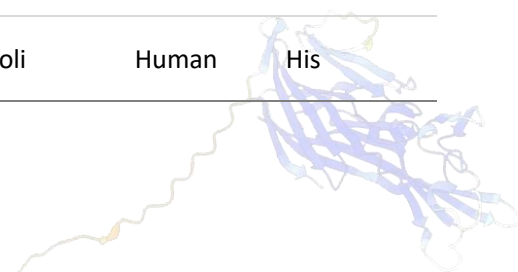
	CCND2-2612H	Recombinant Human CCND2 protein, His & T7-tagged	E. coli	Human	His & T7
	CCND2-894H	Recombinant Human CCND2 protein, Myc/DDK-tagged	HEK293T	Human	Myc/DDK
	CCND2-6157H	Recombinant Human CCND2 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CCND2-20H	Recombinant Human CCND2 protein, GST-tagged	E. coli	Human	GST
CCND3	CCND3-21H	Recombinant Human CCND3 protein, GST-tagged	E. coli	Human	GST
	CCND3-2532H	Recombinant Human CCND3 protein, His-tagged	E. coli	Human	His
	CCND3-839H	Recombinant Human CCND3 protein, GST-tagged	Wheat Germ	Human	GST
	CCND3-840H	Recombinant Human CCND3 protein, His/T7-tagged	E. coli	Human	His/T7
	CCND3-1817H	Recombinant Human CCND3 protein, GST-tagged	E. coli	Human	GST
ARF1	ARF1-9799H	Recombinant Human ARF1, GST-tagged	E.coli	Human	GST
	ARF1-224H	Recombinant Human ARF1, His-tagged	E. coli	Human	His
	ARF1-744H	Recombinant Human ARF1 protein, GST-tagged	Wheat Germ	Human	GST
	ARF1-506H	Recombinant Human ARF1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ARF1-1938H	Recombinant Human ARF1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ARF1-2544H	Recombinant Human ARF1 protein, His-GST & Myc-tagged	E. coli	Human	His-GST & Myc
ARF3	ARF3-237H	Recombinant Human ARF3, His tagged	E. coli	Human	His
	ARF3-6867H	Recombinant Human ADP-Ribosylation Factor 3, His-tagged	E. coli	Human	His
	ARF3-9800H	Recombinant Human ARF3, GST-tagged	E.coli	Human	GST
	ARF3-4840H	Recombinant Human ARF3 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ARF3-745H	Recombinant Human ARF3 protein, GST-tagged	Wheat Germ	Human	GST



ARF4	ARF4-3956H	Recombinant Human ARF4 protein, His-tagged	E. coli	Human	His
	ARF4-746H	Recombinant Human ARF4 protein, GST-tagged	Wheat Germ	Human	GST
	ARF4-6329H	Recombinant Human ARF4 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ARF4-9801H	Recombinant Human ARF4, GST-tagged	E.coli	Human	GST
ARF5	ARF5-9802H	Recombinant Human ARF5, GST-tagged	E.coli	Human	GST
	ARF5-198H	Recombinant Human ARF5, His tagged	E. coli	Human	His
	ARF5-748H	Recombinant Human ARF5 protein, GST-tagged	Wheat Germ	Human	GST
	ARF5-5150H	Recombinant Human ARF5 protein, GST-tagged	E. coli	Human	GST
ARF6	ARF6-749H	Recombinant Human ARF6 protein, GST-tagged	Wheat Germ	Human	GST
	ARF6-26533TH	Recombinant Human ARF6 protein, His-tagged	E. coli	Human	His
	ARF6-2595H	Recombinant Human ARF6 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	ARF6-2545H	Recombinant Human ARF6 protein, His-SUMO-tagged	E. coli	Human	His-SUMO
	ARF6-9803H	Recombinant Human ARF, His-tagged	E.coli	Human	His
ATM	ATM-848H	Recombinant Human ATM	Mammalian Cells	Human	His
	ATM-9987H	Recombinant Human ATM, GST-tagged	E.coli	Human	GST
	ATM-185H	Recombinant Human ATM protein, GST-tagged	Insect cells	Human	GST
	ATM-953H	Recombinant Human ATM protein, GST-tagged	Wheat Germ	Human	GST
	ATM-6852H	Recombinant Human ATM protein, His & GST-tagged	E. coli	Human	His & GST
ATR	ATR-1026H	Recombinant Human ATR protein, GST-tagged	Wheat Germ	Human	GST
	ATR-1768H	Recombinant Human ATR protein, His & T7-tagged	E. coli	Human	His & T7
	ATR-4932H	Recombinant Human ATR Protein, GST-tagged	Insect cells	Human	GST



ATRIP	ATRIP-3456H	Recombinant Human ATRIP Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK	
	ATRIP-1027H	Recombinant Human ATRIP protein, GST-tagged	Wheat Germ	Human	GST	
	ATRIP-10062H	Recombinant Human ATRIP, GST-tagged	E.coli	Human	GST	
CHK1	CHK1-3899H	Recombinant Human CHK1 protein, His-tagged	E. coli	Human	His	
CDK2	CDK2-726H	Recombinant Human CDK2 Protein, His-tagged	E. coli	Human	N-His	
	CDK2-655H	Recombinant Human cyclin-dependent kinase 2, His-tagged	Insect cell	Human	His-tag	
	CDK2-172H	Recombinant Human CDK2	Mammalian Cells	Human	His	
	CDK2-615H	Recombinant Human CDK2, His tagged	Baculovirus-Insect Cells	Human	His	
	CDK2-114H	Recombinant Human CDK2/CyclinO, GST-tagged	Sf9 insect cells using baculovirus	Human	GST	
	CDK2-48H	Recombinant Human CDK2/CCNE1 protein, GST-tagged	Insect cells	Human	GST	
	CDK2-1000H	Recombinant Human CDK2 Protein, GST-Tagged	Wheat Germ	Human	GST	
	CDK2-1003H	Recombinant Human CDK2 Protein, GST-Tagged	Insect Cell	Human	GST	
	CDK2-1933H	Recombinant Human CDK2 protein, His & GST-tagged	E. coli	Human	His & GST	
	CDK2-5392H	Recombinant Human CDK2 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK	
	CDK2-3142H	Recombinant Human CDK2 Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK	
	CDK4	CDK4-3139H	Recombinant Human CDK4 Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
		CDK4-633H	Recombinant Human CDK4 Protein, GST-tagged	Insect cells	Human	GST
CDK4-758HAF488		Recombinant Human CDK4 Protein, GST-tagged, Alexa Fluor 488 conjugated	Insect cells	Human	GST	
CDK4-2678H		Recombinant Human CDK4 protein, His-tagged	E. coli	Human	His	



	CDK4-2208H	Recombinant Human CDK4 protein, His-tagged	Insect Cell	Human	His
	CDK4-1011H	Recombinant Human CDK4 Protein, GST-Tagged	Wheat Germ	Human	GST
	CDK4-1015H	Recombinant Human CDK4 Protein, GST-Tagged	Insect Cell	Human	GST
	CDK4-1016H	Recombinant Human CDK4 Protein, His-Tagged	Insect Cell	Human	His
	CDK4-191H	Recombinant Human CDK4 protein, T7-tagged	E. coli	Human	T7
	CDK4-938H	Recombinant Human CDK4 protein, His/T7-tagged	E. coli	Human	His/T7
	CDK4-27905TH	Recombinant Human CDK4	E. coli		
	CDK4-758H	Recombinant Human CDK4, GST tagged	Baculovirus-Insect Cells	Human	GST
	CDK4-11049H	Recombinant Human CDK4, GST-tagged	E.coli	Human	GST
	CDK4-7156H	Recombinant Human Cyclin-Dependent Kinase 4, His-tagged	E. coli	Human	His
	CDK4-758HAF647	Recombinant Human CDK4 Protein, GST-tagged, Alexa Fluor 647 conjugated	Insect cells	Human	GST
	CDK4-758HF	Recombinant Human CDK4 Protein, GST-tagged, FITC conjugated	Insect cells	Human	GST
	CDK4-758HAF555	Recombinant Human CDK4 Protein, GST-tagged, Alexa Fluor 555 conjugated	Insect cells	Human	GST
CDK6	CDK6-728H	Recombinant Human CDK6 Protein, His-tagged	E. coli	Human	N-His
	CDK6-1537H	Recombinant Human CDK6, Unactive, His-tagged	Sf9 Cells	Human	His
	CDK6-1883H	Recombinant Human CDK6 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CDK6-3246H	Recombinant Human CDK6 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CDK6-1028H	Recombinant Human CDK6 Protein, GST-Tagged	Wheat Germ	Human	GST
	CDK6-1032H	Recombinant Human CDK6 Protein, GST-Tagged	Insect Cell	Human	GST



CCNE1	CCNE1-2926H	Recombinant Human CCNE1 protein, His-tagged	E. coli	Human	His
	CCNE1-27521TH	Recombinant Human CCNE1	Baculovirus infected sf9 cells		
	CCNE1-522H	Recombinant Human CCNE1, Gly & Pro tagged	Baculovirus-Insect cells	Human	Gly & Pro
	CCNE1-3075H	Recombinant Human CCNE1, His tagged	Baculovirus-Insect Cells	Human	His
	CCNE1-11754H	Recombinant Human CCNE1, GST-tagged	E.coli	Human	GST
	CCNE1-0665H	Recombinant Human CCNE1 Protein, GST-Tagged	Wheat Germ	Human	GST
	CCNE1-259H	Recombinant Human CCNE1 Protein, His & GST-tagged	Baculovirus-Insect Cells	Human	His & GST
CCNE2	CCNE2-180H	Recombinant Human CCNE2 protein, GST-tagged	Insect cells	Human	GST
	CCNE2-0667H	Recombinant Human CCNE2 Protein, GST-Tagged	Wheat Germ	Human	GST
	CCNE2-3047H	Recombinant Human CCNE2 protein, His-tagged	E. coli	Human	His
	CCNE2-10864H	Recombinant Human CCNE2, GST-tagged	E.coli	Human	GST
	CCNE2-2774H	Recombinant Human CCNE2 protein, His-tagged	E. coli	Human	His
CDK1	CDK1-653H	Recombinant Human CDK1 protein, His-tagged	E.coli	Human	His
	CDK1-3143H	Recombinant Human CDK1 Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	CDK1-2157H	Recombinant Human CDK1 Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	CDK1-213H	Recombinant Human CDK1 protein, T7/His-tagged	E. coli	Human	T7/His
	CDK1/CyclinB1-48H	Recombinant Human CDK1/CyclinB1, GST-tagged, Active	Insect cells	Human	GST
	CDK1-654H	Recombinant Human cyclin-dependent kinase 1, His-tagged	Insect cell	Human	His-tag

	CDK1-1533H	Recombinant Human CDK1, Unactive, GST-tagged	Sf9 Cells	Human	GST
	CDK1-997H	Recombinant Human CDK1, GST-tagged	E.coli	Human	GST
	CDK1-171H	Recombinant Human CDK1	Mammalian Cells	Human	His
	CDK1-3330H	Recombinant Human CDK1, GST tagged	Baculovirus-Insect Cells	Human	GST
	CDK1-31590TH	Recombinant Human Human CDK1	Baculovirus infected sf9 cells		
	CDK1-31592TH	Recombinant Human Human CDK1	Baculovirus infected sf9 cells		
CDC2	CDC2-0904H	Recombinant Human CDC2 Protein, GST-Tagged	Wheat Germ	Human	GST
	CDC2-0906H	Recombinant Human CDC2 Protein, GST-Tagged	Insect Cell	Human	GST
	CDC2-0907H	Recombinant Human CDC2 Protein, GST-His-Tagged	Insect Cell	Human	GST-His
PCNA	PCNA-110H	Recombinant Human PCNA Protein, His-tagged	E. coli	Human	His
	PCNA-626H	Recombinant Human PCNA Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
	PCNA-1535H	Recombinant Human PCNA protein	E. coli	Human	
	PCNA-5685H	Recombinant Human PCNA Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
	PCNA-6999H	Recombinant Human PCNA, His tagged	Baculovirus-Insect Cells	Human	His
	PCNA-4863H	Recombinant Human PCNA, His-tagged	E. coli	Human	His
	PCNA-4863	Recombinant Human PCNA protein, His-tagged	E. coli	Human	His
GADD45A	GADD45A-13109H	Recombinant Human GADD45A, GST-tagged	E.coli	Human	GST
	GADD45A-3880H	Recombinant Human GADD45A, His & GST tagged	Baculovirus-Insect Cells	Human	His & GST

GADD45A-4657H	Recombinant Human GADD45A Protein, GST-tagged	Wheat Germ	Human	GST
GADD45A-941H	Recombinant Human GADD45A Protein, MYC/DDK-tagged	HEK293	Human	MYC/DDK
GADD45A-1993H	Recombinant Human GADD45A Protein, Myc/DDK-tagged, C13 and N15-labeled	HEK293	Human	Myc/DDK
GADD45A-3482H	Recombinant Human GADD45A protein, His-tagged	E. coli	Human	His
GADD45A-2936H	Recombinant Human GADD45A protein, His-SUMO-tagged	E. coli	Human	His-SUMO



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