



Recombinant Human RAF proto-oncogene serine/threonine-protein kinase (RAF1)

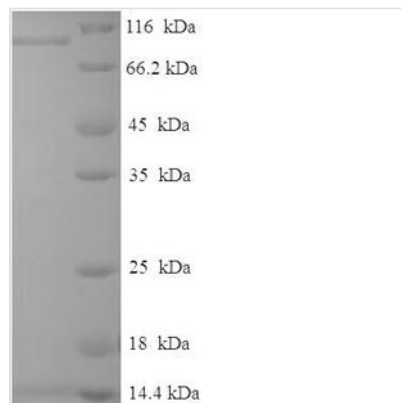
Product Code	CSB-EP019284HU
Relevance	<p>Serine/threonine-protein kinase that acts as a regulatory link between the mbrane-associated Ras GTPases and the MAPK/ERK cascade, and this critical regulatory link functions as a switch determining cell fate decisions including proliferation, differentiation, apoptosis, survival and oncogenic transformation. RAF1 activation initiates a mitogen-activated protein kinase (MAPK) cascade that comprises a sequential phosphorylation of the dual-specific MAPK kinases (MAP2K1/MEK1 and MAP2K2/MEK2) and the Extracellular domain signal-regulated kinases (MAPK3/ERK1 and MAPK1/ERK2). The phosphorylated form of RAF1 (on residues Ser-338 and Ser-339, by PAK1) phosphorylates BAD/Bcl2-antagonist of cell death at 'Ser-75'. Phosphorylates adenylyl cyclases: ADCY2, ADCY5 and ADCY6, resulting in their activation. Phosphorylates PPP1R12A resulting in inhibition of the phosphatase activity. Phosphorylates TNNT2/cardiac muscle troponin T. Can promote NF-kB activation and inhibit signal transducers involved in motility (ROCK2), apoptosis (MAP3K5/ASK1 and STK3/MST2), proliferation and angiogenesis (RB1). Can protect cells from apoptosis also by translocating to the mitochondria where it binds BCL2 and displaces BAD/Bcl2-antagonist of cell death. Regulates Rho signaling and migration, and is required for normal wound healing. Plays a role in the oncogenic transformation of epithelial cells via repression of the TJ protein, occludin (OCLN) by inducing the up-regulation of a transcriptional repressor SNAI2/SLUG, which induces down-regulation of OCLN. Restricts caspase activation in response to selected stimuli, notably Fas stimulation, pathogen-mediated macrophage apoptosis, and erythroid differentiation</p>
Storage	<p>The shelf life is related to many factors, storage state, buffer ingredients, storage temperature and the stability of the protein itself. Generally, the shelf life of liquid form is 6 months at -20°C/-80°C. The shelf life of lyophilized form is 12 months at -20°C/-80°C.</p>
Uniprot No.	P04049
Alias	Proto-oncogene c-RAF ;cRafRaf-1
Product Type	Recombinant Protein
Immunogen Species	Homo sapiens (Human)
Purity	Greater than 90% as determined by SDS-PAGE.
Sequence	<p>MEHIQGAWKTISNGFGFKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTDPSPK TSNTIRVFLPNKQRTVVNVRNGMSLHDCMKALKVRGLQPECCAVFRLLEHKK GKKARLDWNTDAASLIGEELQVDFLDHVPLTTHNFARKTFLKLAFCDICQKFL NGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNSTIGDSGVPA PSLT MRRMRESVSRMPVSSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVH MVSTTLPVDSRMIEDAIRSHSESASPSALSSSPNNLSPTGWSQPKTPVPAQRE RAPVSGTQEKNKIRPRGQRDSSYYWEIEASEVMLSTRIGSGSFGTVYKGKWH GDVAVKILKVVDPTPEQFQAFRNEVAVLRKTRHVNILLFMGYMTKDNLAIVTQ</p>



WCEGSSLYKHLHVQETKFQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFL
HEGLTVKIGDFGLATVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDNNPFSF
QSDVYSYGIVLYELMTGELPYSHINNRDQIIFMVGRGYASPDLSKLYKNCPKAM
KRLVADCVKVKKEERPLFPQILSSIPELLQHSLPKINRSASEPSLHRAAHTEDINA
CTLTTSPRLPVF

Lead Time	3-7 business days
Research Area	Cancer
Source	E.coli
Gene Names	RAF1
Expression Region	1-648aa
Notes	Repeated freezing and thawing is not recommended. Store working aliquots at 4°C for up to one week.
Tag Info	N-terminal 6xHis-SUMO-tagged
Mol. Weight	89.1kDa
Protein Description	Full Length

Image



(Tris-Glycine gel) Discontinuous SDS-PAGE (reduced) with 5% enrichment gel and 15% separation gel.

Description

The recombinant human RAF1 protein, engineered with an N-terminal 6xHis-SUMO tag, is expressed using an E. coli expression system. The RAF1 gene fragment (1-648aa) is first co-cloned into a suitable expression vector with the 6xHis-SUMO tag gene and then transformed into competent E. coli cells. After induction with IPTG to trigger protein expression, the cells are harvested and lysed to obtain the targeted proteins. The recombinant RAF1 protein is purified using affinity chromatography. The purified RAF1 protein is analyzed for purity via SDS-PAGE, which typically shows a purity greater than 90%, ensuring the protein is suitable for downstream applications.

The human RAF1 (C-Raf) is a critical component of the MAPK signaling pathway. This pathway is essential for various cellular processes, including proliferation, differentiation, and survival. RAF1 is a serine/threonine kinase activated by the small GTPase Ras, which is itself stimulated by growth factors, hormones, and cytokines [1-4]. Upon activation, RAF1 phosphorylates and activates MEK, which subsequently activates ERK, leading to a cascade of downstream signaling events that influence gene expression and cellular



responses [5-7].

Excessive or prolonged activation of RAF1 can lead to adverse cellular outcomes, including apoptosis or uncontrolled cell division [8][9]. Recent studies have also highlighted the role of RAF1 in crosstalk with other signaling pathways, such as the PI3K/Akt pathway, which further complicates its function in cancer biology [2][10]. Understanding the multifaceted roles of RAF1 and its interactions within signaling networks is crucial for developing targeted therapies aimed at inhibiting its activity in cancer treatment [11][12].

References:

- [1] M. Garnett and R. Marais, Guilty as charged, *Cancer Cell*, vol. 6, no. 4, p. 313-319, 2004. <https://doi.org/10.1016/j.ccr.2004.09.022>
- [2] Q. Li, Z. Li, T. Luo, & H. Shi, Targeting the pi3k/akt/mtor and raf/mek/erk pathways for cancer therapy, *Molecular Biomedicine*, vol. 3, no. 1, 2022. <https://doi.org/10.1186/s43556-022-00110-2>
- [3] R. Galuppo, D. Ramaiah, O. Ponte, & R. Gedaly, Molecular therapies in hepatocellular carcinoma: what can we target?, *Digestive Diseases and Sciences*, vol. 59, no. 8, p. 1688-1697, 2014. <https://doi.org/10.1007/s10620-014-3058-x>
- [4] V. Balan, D. Leicht, J. Zhu, K. Balan, A. Kaplun, V. Singh?Gupta, et al. Identification of novel in vivo raf-1 phosphorylation sites mediating positive feedback raf-1 regulation by extracellular signal-regulated kinase, *Molecular Biology of the Cell*, vol. 17, no. 3, p. 1141-1153, 2006. <https://doi.org/10.1091/mbc.e04-12-1123>
- [5] C. Bondzi, S. Grant, & G. Krystal, A novel assay for the measurement of raf-1 kinase activity, *Oncogene*, vol. 19, no. 43, p. 5030-5033, 2000. <https://doi.org/10.1038/sj.onc.1203862>
- [6] H. Park, S. Hwang, & K. Baek, Usp7 regulates the erk1/2 signaling pathway through deubiquitinating raf-1 in lung adenocarcinoma, *Cell Death and Disease*, vol. 13, no. 8, 2022. <https://doi.org/10.1038/s41419-022-05136-6>
- [7] K. Yeung, P. Janosch, B. McFerran, D. Rose, H. Mischak, J. Sedivy, et al. Mechanism of suppression of the raf/mek/extracellular signal-regulated kinase pathway by the raf kinase inhibitor protein, *Molecular and Cellular Biology*, vol. 20, no. 9, p. 3079-3085, 2000. <https://doi.org/10.1128/mcb.20.9.3079-3085.2000>
- [8] J. Chen, K. Fujii, L. Zhang, T. Roberts, & H. Fu, Raf-1 promotes cell survival by antagonizing apoptosis signal-regulating kinase 1 through a mek-erk independent mechanism, *Proceedings of the National Academy of Sciences*, vol. 98, no. 14, p. 7783-7788, 2001. <https://doi.org/10.1073/pnas.141224398>
- [9] S. Jin, Y. Zhuo, W. Guo, & J. Field, P21-activated kinase 1 (pak1)-dependent phosphorylation of raf-1 regulates its mitochondrial localization, phosphorylation of bad, and bcl-2 association, *Journal of Biological Chemistry*, vol. 280, no. 26, p. 24698-24705, 2005. <https://doi.org/10.1074/jbc.m413374200>
- [10] D. Reverter, D. Matallanas, G. Weitsman, C. Preisinger, T. Ng, & W. Köhler, Proapoptotic kinase mst2 coordinates signaling crosstalk between rassf1a, raf-1, and akt, *Cancer Research*, vol. 70, no. 3, p. 1195-1203, 2010. <https://doi.org/10.1158/0008-5472.can-09-3147>
- [11] D. Ritt, M. Abreu-Blanco, L. Bindu, D. Durrant, M. Zhou, S. Specht, et al. Inhibition of ras/raf/mek/erk pathway signaling by a stress-induced phosphoregulatory circuit, *Molecular Cell*, vol. 64, no. 5, p. 875-887, 2016.



<https://doi.org/10.1016/j.molcel.2016.10.029>

[12] H. Shi, X. Kong, A. Ribas, & R. Lo, Combinatorial treatments that overcome pdgfr β -driven resistance of melanoma cells to v600eb-raf inhibition, Cancer Research, vol. 71, no. 15, p. 5067-5074, 2011.

<https://doi.org/10.1158/0008-5472.can-11-0140>

Reconstitution

We recommend that this vial be briefly centrifuged prior to opening to bring the contents to the bottom. Please reconstitute protein in deionized sterile water to a concentration of 0.1-1.0 mg/mL. We recommend to add 5-50% of glycerol (final concentration) and aliquot for long-term storage at -20°C/-80°C. Our default final concentration of glycerol is 50%. Customers could use it as reference.