

KRAS kot potencialna, a zahtevna tarča za PROTAC terapijo-REŠITVE

V raziskovalnem laboratoriju preučujejo potencialne tarče za zdravljenje rakavih obolenj z uporabo tehnologije PROTAC (proteolysis-targeting chimeras), ki omogoča usmerjeno razgradnjo proteinov. PROTAC je molekula, sestavljena iz treh osnovnih komponent: liganda za tarčni protein, povezovalca (linkerja) in liganda za E3 ubikvitin ligazo, ki posreduje prenos aktiviranega ubikvitina z E2 na specifičen substratni protein. Ligand za tarčni protein selektivno veže protein interesa (POI), ligand za E3 ligazo pa rekrutira E3 ubikvitin ligazo. Tvori se ternarni kompleks POI-PROTAC-E3 ligaza, v katerem E3 ligaza ubikvitinira POI, kar ga označi za razgradnjo v proteasomu.

Tvoja raziskovalna skupina je izolirala neznano aminokislinsko zaporedje proteina iz tumorskega vzorca, za katerega sumiš, da ima vlogo pri razvoju raka. Tvoja naloga je, da protein identificiraš, analiziraš njegove značilnosti ter oceniš njegovo primernost kot potencialno PROTAC tarčo.

Identifikacija proteina in ocena aktualnosti

1. Proteinu pripadajoče zaporedje je pripeto spodaj.

1. Identificiraj protein, ki ga kodira dano zaporedje, in

Gre za KRAS protein.

Informacijo o tem najdeš z iskanjem z zaporedjem po pblastu:

Descriptions		Graphic Summary	Alignments	Taxonomy				
Sequences producing significant alignments				Download	Select columns	Show	100	?
select all 100 sequences selected				GenPept	Graphics	Distance tree of results	Multiple alignment	MSA Viewer
Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
<input checked="" type="checkbox"/> GTPase KRas isoform a [Homo sapiens]	Homo sapiens	390	390	100%	8e-137	100.00%	189	NP_001356715.1
<input checked="" type="checkbox"/> GTPase KRas isoform X3 [Cavia porcellus]	Cavia porcellus	392	392	100%	1e-136	100.00%	227	XP_003470499.2
<input checked="" type="checkbox"/> GTPase KRas isoform X1 [Gorilla gorilla gorilla]	Gorilla gorilla gorilla	391	391	100%	1e-136	100.00%	207	XP_063550180.1
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	390	390	100%	1e-136	100.00%	190	TVVR_A
<input checked="" type="checkbox"/> GTPase KRas isoform X3 [Chlorocebus sabaeus]	Chlorocebus sabaeus	392	392	100%	1e-136	100.00%	227	XP_007966155.1
<input checked="" type="checkbox"/> PREDICTED: GTPase KRas isoform X1 [Bison bison bison]	Bison bison bison	390	390	100%	1e-136	99.47%	189	XP_010854295.1
<input checked="" type="checkbox"/> GTPase KRas isoform X3 [Desmodus rotundus]	Desmodus rotundus	391	391	100%	2e-136	99.47%	227	XP_053777690.1
<input checked="" type="checkbox"/> GTPase KRas isoform X3 [Neophocaena asiaorientalis asiaorientalis]	Neophocaena asiaorientalis asiaorientalis	391	391	100%	2e-136	99.47%	227	XP_024588800.1
<input checked="" type="checkbox"/> GTPase KRas isoform 1-T1 [Rhinopoma microphyllum]	Rhinopoma microphyllum	392	392	100%	2e-136	99.47%	236	KAN3855304.1
<input checked="" type="checkbox"/> KRAS isoform 4 [Pongo abelii]	Pongo abelii	390	390	100%	2e-136	99.47%	189	PNJ03835.1
<input checked="" type="checkbox"/> GTPase KRas isoform X1 [Marmota marmota marmota]	Marmota marmota marmota	390	390	100%	2e-136	99.47%	189	XP_015353728.1
<input checked="" type="checkbox"/> GTPase KRas isoform X4 [Gorilla gorilla gorilla]	Gorilla gorilla gorilla	392	392	100%	2e-136	100.00%	245	XP_063550183.1
<input checked="" type="checkbox"/> GTPase KRas isoform X3 [Echinops telfairi]	Echinops telfairi	391	391	100%	2e-136	99.47%	227	XP_004700038.1

2. preveri, ali ima znano strukturo.

Njegova struktura je znana. To preverimo z iskanjem s pblastom po PDB.

Job Title: Protein Sequence

RID: ZSY9X64K016 Search expires on 05-08 19:36 pm [Download All](#) v

Program: BLASTP [Citation](#) v

Database: pdb [See details](#) v

Query ID: Icl|Query_5582333

Description: unnamed protein product

Molecule type: amino acid

Query Length: 189

Other reports: [Distance tree of results](#) [Multiple alignment](#) [MSA viewer](#) ?

Filter Results

Organism: only top 20 will appear exclude

Type common name, binomial, taxid or group name

+ [Add organism](#)

Percent Identity: to E value: to Query Coverage: to

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Descriptions | Graphic Summary | Alignments | Taxonomy

Sequences producing significant alignments Download v Select columns v Show 100 v ?

select all 100 sequences selected [GenPept](#) [Graphics](#) [Distance tree of results](#) [Multiple alignment](#) [MSA Viewer](#)

Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per Ident	Acc Len	Accession
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	390	390	100%	1e-140	100.00%	190	7VVB_A
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	365	365	94%	8e-131	100.00%	178	8T71_A
<input checked="" type="checkbox"/> Chain B_GTPase KRas [Homo sapiens]	Homo sapiens	362	362	94%	2e-129	99.44%	178	8T71_B
<input checked="" type="checkbox"/> Chain A_GTPase KRas_N-terminally processed [Homo sapiens]	Homo sapiens	348	348	89%	6e-124	99.41%	169	8JHL_A
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	348	348	89%	6e-124	99.41%	172	9G0Y_A
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	347	347	89%	9e-124	99.41%	170	8T73_A
<input checked="" type="checkbox"/> Chain A_GTPase KRas [Homo sapiens]	Homo sapiens	347	347	89%	1e-123	99.41%	169	8JGD_A

Protein KRAS ima pomembno vlogo pri uravnavanju celične proliferacije in signalnih poteh ter je pogosto mutiran pri različnih vrstah raka, zato predstavlja pomembno tarčo sodobnih protirakovih terapij.

Odgovore na vprašanja iz sledeče naloge od 2. dalje najdeš z iskanjem po PubMed-u.

2. Preveri koliko je vseh člankov, ki so bili objavljeni na temo proteina KRAS.

32084

An official website of the United States government [Here's how you know](#) v

NIH National Library of Medicine
National Center for Biotechnology Information [Log in](#)

PubMed® KRAS [Search](#)

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32,084 results [Page 1 of 3,209](#)

RESULTS BY YEAR

PUBLICATION DATE

1 year 5 years

KRAS mutation in pancreatic cancer.
1 Luo J.
Cite Semin Oncol. 2021 Feb;48(1):10-18. doi: 10.1053/j.seminoncol.2021.02.003. Epub 2021 Feb 23.
PMID: 33676749 [Free PMC article](#). [Review](#).
More recently, covalent inhibitors targeting the **KRAS**(G12C) oncoprotein have been developed. These inhibitors showed promising activity in **KRAS**(G12C) mutant pancreatic cancer in early clinical trials. This review will present an updated summary of our understanding ...

Targeting KRAS in pancreatic cancer.
2 Stickler S, Rath B, Hamilton G.
Cite Oncol Res. 2024 Apr 23;32(5):799-805. doi: 10.32604/or.2024.045356. eCollection 2024.
PMID: 38686056 [Free PMC article](#). [Review](#).
However, the most common **KRAS** mutations in PDAC are G12D (44%), G12V (34%) and G12R (20%) that

3. Ali gre za aktualno raziskovalno področje?

Da, v zadnjih letih število objavljenih člankov na leto narašča.

4. Koliko člankov je takih, kjer se ime proteina pojavi že v samem naslovu ali povzetku članka?

30808

PubMed® (KRAS[Title/Abstract]) AND (KRAS[Title/Abstract]) Search

Advanced Create alert Create RSS User Guide

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RESULTS BY YEAR

PUBLICATION DATE

1 year
 5 years
 10 years
 Custom Range

TEXT AVAILABILITY

Abstract

30,808 results Page 1 of 3,081

Defining the KRAS- and ERK-dependent transcriptome in KRAS-mutant cancers.
1 Klomp JA, Klomp JE, Stalneckner CA, Bryant KL, Edwards AC, Drizyte-Miller K, Hibshman PS, Diehl JN, Lee YS, Morales AJ, Taylor KE, Peng S, Tran NL, Herring LE, Prevatte AW, Barker NK, Hover LD, Hallin J, Sorokin A, Kanikarla PM, Chowdhury S, Coker O, Lee HM, Goodwin CM, Gautam P, Olson P, Christensen JG, Shen JP, Kopetz S, Graves LM, Lim KH, Wang-Gillam A, Wennerberg K, Cox AD, Der CJ. Science. 2024 Jun 7;384(6700):eadk0775. doi: 10.1126/science.adk0775. Epub 2024 Jun 7. PMID: 38843331 **Free PMC article.**
Unexpectedly, our **KRAS**-dependent gene signature diverges substantially from the frequently cited Hallmark **KRAS** signaling gene signature, is driven predominantly through the ERK mitogen-activated protein kinase (MAPK) cascade, and accurately reflects **KRAS**- and ...

Oncogenic KRAS Drives Lipofibrogenesis to Promote Angiogenesis and Colon Cancer Progression.
2 Hsu WH, LaBella KA, Lin Y, Xu P, Lee R, Hsieh CE, Yang L, Zhou A, Blecher JM, Wu CJ, Lin K, Shang X, Jiang S, Spring DJ, Xia Y, Chen P, Shen JP, Kopetz S, DePinho RA. Cancer Discov. 2023 Dec 12;13(12):2652-2673. doi: 10.1158/2159-8290.CD-22-1467. PMID: 37768068 **Free PMC article.**
Oncogenic **KRAS** (**KRAS***) contributes to many cancer hallmarks. In colorectal cancer, **KRAS*** suppresses

5. Koliko člankov je bilo z omenjenim proteinom objavljenih v letu 2026?

1245

PubMed® (KRAS) AND (\"2026/1/1\"[Date - Publication] : \"3000\"[Date - Publication]) Search

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RESULTS BY YEAR

PUBLICATION DATE

1 year
 5 years
 10 years
 Custom Range

TEXT AVAILABILITY

Abstract

1,245 results Page 1 of 125

MAPK-driven epithelial cell plasticity drives colorectal cancer therapeutic resistance.
1 White M, Mills ML, Millett LM, Gilroy K, Hong Y, Zeiger LB, Simpson RJ, Corry SM, Ligeza A, Lannagan TRM, Susanti S, Ridgway RA, Yazgili AS, Grzesiak L, Amirkhah R, Ford CA, Vlahov N, Tovell H, Officer-Jones L, Ficken C, Pennie R, Najumudeen AK, Raven A, Nasreddin N, Chauhan E, Papanastasiou AS, Nixon C, Morrison V, Jackstadt R, Graham JS, Miller CJ, Ross SJ, Barry ST, Pavet V, Wilson RH, Le Quesne J, Dunne PD, Tejpar S, Leedham S, Campbell AD, Sansom OJ. Nature. 2026 Feb;650(8102):748-758. doi: 10.1038/s41586-025-09916-w. Epub 2025 Nov 24. PMID: 41286180 **Free PMC article.**
Although oncogenic MAPK signalling in CRC is common, with frequent mutations of both **KRAS** (40-50%) and BRAF (10%)(1), inhibition of this pathway typically drives resistance clinically. Here, given the development of **KRAS** inhibitors and licensing of BRAF inhibitor co ...

Emerging landscape of KRAS inhibitors in cancer treatment.
2 Riedl JM, Matsubara H, McNeil R, Patel PS, Fece de la Cruz F, Gulhan DC, Corcoran RB. Cancer Cell. 2026 Mar 9;44(3):471-497. doi: 10.1016/j.ccell.2026.01.001. Epub 2026 Jan 29. PMID: 41616774 **Free article.** Review.
Alterations in **KRAS**, NRAS, and HRAS occur in roughly 20% of patients with cancer, making RAS one of the most intensively studied oncogenic targets. The discovery of mutant-selective **KRAS**(G12C) inhibitors

6. Koliko člankov pa je takih, ki so pregledni in hkrati vsebujejo tako besedo *KRAS* kot tudi *PROTAC*?

44

PublMed® (KRAS) AND (protac) Search

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MY CUSTOM FILTERS 44 results Page 1 of 5

RESULTS BY YEAR

Filters applied: Review. [Clear all](#)

KRAS: Biology, Inhibition, and Mechanisms of Inhibitor Resistance.
1 Ash LJ, Busia-Bourdain O, Okpattah D, Kamel A, Liberchuk A, Wolfe AL.
Cite Curr Oncol. 2024 Apr 3;31(4):2024-2046. doi: 10.3390/currncol31040150.
PMID: 38668053 [Free PMC article](#). Review.
KRAS is a small GTPase that is among the most commonly mutated oncogenes in cancer. Here, we discuss **KRAS** biology, therapeutic avenues to target it, and mechanisms of resistance that tumors employ in response to **KRAS** inhibition. Several strategies are under i ...

Targeting KRAS in pancreatic cancer.
2 Stickler S, Rath B, Hamilton G.
Cite Oncol Res. 2024 Apr 23;32(5):799-805. doi: 10.32604/or.2024.045356. eCollection 2024.
PMID: 38686056 [Free PMC article](#). Review.
However, the most common **KRAS** mutations in PDAC are G12D (44%), G12V (34%) and G12R (20%) that are not amenable to treatment by **KRAS** G12C-directed cysteine-reactive **KRAS** inhibitors such as Sotorasib and Adagrasib that exhibit clinical efficacy in lung cancer. ...

PUBLICATION DATE

1 year
 5 years
 10 years
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TEXT AVAILABILITY

7. V katerem letu sta bila izdana le dva taka članka (pregledna, hkrati pa vsebujeta besedi *KRAS* in *PROTAC*)?
2022 (razvidno iz levega diagrama).

Značilnosti identificiranega proteina

1. Kje v celici oziroma izven nje v človeku najdemo protein KRAS? Gre morda za transmembranski protein?
Protein se nahaja v celični membrani in citoplazmi. Ne gre za transmembranski protein.

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced | List Search Help

Function Entry Variant viewer 722 Feature viewer Genomic coordinates Publications External links History

Subcellular Location

UniProt Annotation GO Annotation

Cell membrane 3 Publications; Lipid-anchor 1 Publication 1 Publication
Endomembrane system 1 Publication
Cytoplasm, cytosol 1 Publication

Isoform 2B
Cell membrane 1 Publication; Lipid-anchor 1 Publication

2. Koliko aminokislinskih ostankov tvori ta protein?

189

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced | List Search Help

Function Variant viewer 223 Feature viewer Genomic coordinates Publications External links History

P01116-1
This isoform has been chosen as the **canonical** sequence. All positional information in this entry refers to it. This is also the sequence that appears in the downloadable versions of the entry.

Name 2A
Synonyms K-Ras4A 1 Publication
See also sequence in UniParc or sequence clusters in UniRef

Tools + Download 49 Add Highlight Copy sequence

Length 189
Mass (law) 21,000

Last updated 1986-07-21 v1
MD5 Checksum 4A8C310887927CECC35B9DE4B784596E

MTEYKLVVVG AGGVGKSALT IQLIQNHFVD EYDPTIEDSY RKQVVIDGET CLLDLDTAG QEEYSAMRDQ YMRGTGEGFLC VFAINNTKSF EDIHYHREIQI KRVKDSQEDVP

MVLVGNKCDL PSRTVDTKQA QDLARSYGIP FIETSAKTRQ RVEDAFYTLV REIRQYRLKK ISKEEKTGCV KIKKCIIM

P01116-2
Name 2B
Synonyms K-Ras4B
See also sequence in UniParc or sequence clusters in UniRef

Differences from canonical 151-153: RVE → GVD 5 Publications
165-189: QYRLKIKSKEEKTGCVKIKKCIIM →
KHKEKMSKDGKSKKSKTKCVIM 5 Publications

Show sequence

3. Iz koliko domen je sestavljen ta protein?

Informacijo najdeš v Prosite. Sestavljen je iz ene, RAS domene.

P01116 RASK_HUMAN (189 aa)
GTPase KRas. *Homo sapiens* (Human)

MTEYKLVVVGAGGVGKSALTIQLIQNHFVDEYDPTIEDSYRKQVVIDGETCLLDLDTAGQEEYSA
MRDQYMRGTGEGFLCVFAINNTKSFEDIHYHREIKRVKDSQEDVPMVLVGNKCDLPSRTVDTKQAQD
LARSYGIPFIETSAKTRQRVEDAFYTLVREIRQYRLKKISKEEKTGCVKIKKCIIM

Legend:

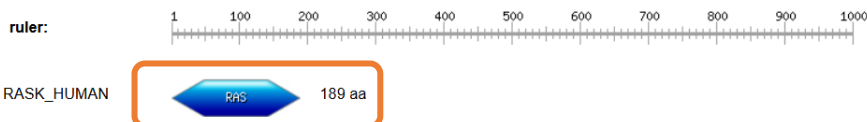
disulfide bridge active site other 'ranges' other sites

Please note that the graphical representations of domains displayed hereafter are for illustrative purposes only, and that their colors and shapes are not intended to indicate homology or shared function.

For more information about how these graphical representations are constructed, go to <https://prosite.expasy.org/mydomains/>.

hits by profiles: [1 hit (by 1 profile) on 1 sequence]

Upper case represents match positions, lower case insert positions, and the '-' symbol represents deletions relative to the matching profile.



GTPase KRas. *Homo sapiens* (Human)

Hits of PS51421 on AlphaFold-P01116-F1-v4

PS51421 RAS Small GTPase Ras domain profile:

Hits of PS51421 on PDB 3D structures x-referenced by P01116: pdb_00002msc_B, pdb_00002msd_B, pdb_00002mse_B, pdb_00003gft_A, pdb_00003gft_B, pdb_00003gft_C, pdb_00003gft_D, pdb_00003gft_E, pdb_00003gft_F, pdb_00004dsn_A, pdb_00004dso_A, pdb_00004epr_A, pdb_00004ept_A, pdb_00004epv_A, pdb_00004epw_A, pdb_00004epx_A, pdb_00004epy_A, pdb_00004i8g_A, pdb_00004ldj_A, pdb_00004lpk_A, pdb_00004lpk_B, pdb_00004lrw_A, pdb_00004lrw_B, pdb_00004luc_A, pdb_00004luc_B, pdb_00004lv6_A, pdb_00004lv6_B, pdb_00004lyf_A, pdb_00004lyf_B, pdb_00004lyf_C, pdb_00004lyh_A, pdb_00004lyh_B, pdb_00004lyh_C, pdb_00004lyj_A, pdb_00004m1o_A, pdb_00004m1o_B, pdb_00004m1o_C, pdb_00004m1s_A, pdb_00004m1s_B, pdb_00004m1s_C, pdb_00004m1t_A, pdb_00004m1t_B, pdb_00004m1t_C, pdb_00004m1w_A, pdb_00004m1w_B, pdb_00004m1w_C, pdb_00004m1y_A, pdb_00004m1y_B, pdb_00004m1y_C, pdb_00004m21_A, pdb_00004m21_B, pdb_00004m21_C, pdb_00004m22_A, pdb_00004m22_B, pdb_00004m22_C, pdb_00004nmm_A, pdb_00004obe_A, pdb_00004obe_B, pdb_00004pzy_A, pdb_00004pzy_B, pdb_00004pzz_A, pdb_00004q01_A, pdb_00004q01_B, pdb_00004q02_A, pdb_00004q03_A, pdb_00004q13_A,

4. V potencialni razvoj katerega raka je vključen? Podatek poiščite v UniProt-u.

V razvoja raka želodca.

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced | List Search Help

Function Variant viewer **722** Feature viewer Genomic coordinates Publications External links History

Gastric cancer (GASC)

Note The disease is caused by variants affecting the gene represented in this entry

Description A malignant disease which starts in the stomach, can spread to the esophagus or the small intestine, and can extend through the stomach wall to nearby lymph nodes and organs. It also can metastasize to other parts of the body. The term gastric cancer or gastric carcinoma refers to adenocarcinoma of the stomach that accounts for most of all gastric malignant tumors. Two main histologic types are recognized, diffuse type and intestinal type carcinomas. Diffuse tumors are poorly differentiated infiltrating lesions, resulting in thickening of the stomach. In contrast, intestinal tumors are usually exophytic, often ulcerating, and associated with intestinal metaplasia of the stomach, most often observed in sporadic disease.

See also MIM:613659

Natural variants in GASC

VARIANT ID	POSITION(S)	CHANGE	DESCRIPTION
VAR_064849	5	K>N	in GASC; found also in a patient with Costello syndrome; exhibits only minor alterations in its in vitro biochemical behavior compared to wild-type protein; dbSNP:rs104894361 1 Publication
VAR_016026	12	G>D	in GASC, JMML and SFM; somatic mutation; also found in pancreatic carcinoma and lung carcinoma; also found in metastatic colorectal cancer; dbSNP:rs121913529 7 Publications
VAR_016028	12	G>S	in GASC and JMML; also found in lung carcinoma; somatic mutation; dbSNP:rs121913530 4 Publications

5. Ali protein vsebuje signalni peptid? Se (tudi) kateri drug del zaporedja v zreli obliki peptida odcepi?

Protein ne vsebuje signalnega peptida,

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced | List Search Help

Function Variant viewer **722** Feature viewer Genomic coordinates Publications External links History

1 30

R T E Y K L V V V G A G G V G K S A L T I Q L I Q N H F V D

TYPE	ID	POSITION(S)	SOURCE	DESCRIPTION
Initiator methionine		1	UniProt	Removed; alternate 1 Publication
Modified residue		1	UniProt	N-acetylmethionine; in GTPase KRas; alternate 1 Publication
Chain	PRO_0000082641	1-186	UniProt	GTPase KRas Tools Add
Modified residue		2	UniProt	N-acetylthreonine; in GTPase KRas, N-terminally processed 1 Publication

Post-translational modification¹

vsebuje pa propeptid, ki v zreli obliki proteina ni prisoten.

UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB Advanced | List Search Help

Function Variant viewer **722** Feature viewer Genomic coordinates Publications External links History

145 189

S A K T R Q R V E D A F Y T L V R E I R Q Y R L K K I S K E E K T P G C V K I K K C I I H

TYPE	ID	POSITION(S)	SOURCE	DESCRIPTION
Lipidation		185	UniProt	1 Publication
Modified residue		186	UniProt	Cysteine methyl ester 1 Publication Combined Sources
Lipidation		186	UniProt	S-farnesyl cysteine 1 Publication 1 Publication Combined Sources
Propeptide	PRO_0000281291	187-189	UniProt	Removed in mature form 1 Publication Tools Add

Post-translational modification¹

6. Katera posttranslacijska modifikacija je najbolj pogosta na C-terminalnem koncu proteina?

Lipidacija.

TYPE	ID	POSITION(S)	SOURCE	DESCRIPTION
Lipidation		182	UniProt	N6-palmitoyl lysine
Lipidation		184	UniProt	N6-palmitoyl lysine
Lipidation		185	UniProt	N6-palmitoyl lysine
Modified residue		186	UniProt	Cysteine methyl ester
Lipidation		186	UniProt	S-farnesyl cysteine

Post-translational modification¹

7. Kaj povzroči glikozilacijo Thr35?

Toksin TcsL (iz bakterije *Paenibacillus sordellii*).

TYPE	POSITION(S)	SOURCE	DESCRIPTION
Glycosylation	35	UniProt	(Microbial infection) O-linked (Glc) threonine; by P.sordellii toxin TcsL.
Modified residue (large scale data)	39	PRIDE	

Post-translational modification¹

Acetylation at Lys-104 prevents interaction with guanine nucleotide exchange factors (GEFs). ^{2 Publications}

Palmitoylated at Lys-182, Lys-184 and Lys-185 (PubMed:29239724).

Palmitoylation on lysine residues is promoted by palmitoylation at Cys-180 (PubMed:29239724).

Lysine-depalmitoylation by SIRT2 promotes its localization to endomembranes in endocytic pathways (PubMed:29239724). ^{1 Publication}

Ubiquitinated by the BCR(LZTR1) E3 ubiquitin ligase complex at Lys-170 in a non-degradative manner, leading to inhibit Ras signaling by decreasing Ras association with membranes. ^{2 Publications}

(Microbial infection) Glucosylated at Thr-35 by P.sordellii toxin TcsL. ^{1 Publication}

Keywords¹

8. S katero metodo je bilo določeno največ struktur tega proteina?

Z XRD.

SOURCE	IDENTIFIER	ISOFORM	METHOD	RESOLUTION	CHAIN	POSITIONS	LINKS
PDB	1D8D		X-ray	2.00 Å	P	178-188	PDB - RCSB-PDB - PDBj - PDBsum - Foldseek
PDB	1D8E		X-ray	3.00 Å	P	178-188	PDB - RCSB-PDB - PDBj - PDBsum - Foldseek
PDB	1KZO		X-ray	2.20 Å	C	169-173	PDB - RCSB-PDB - PDBj - PDBsum - Foldseek
PDB	1KZP		X-ray	2.10 Å	C	169-173	PDB - RCSB-PDB - PDBj - PDBsum - Foldseek

3D structure databases

AlphaFoldDB | P01116 [↗](#) | SASBDB | P01116 [↗](#)

BMRB | P01116 [↗](#) | SMR | P01116 [↗](#)

EMDB | EMD-18657 [↗](#) | ModBase | Search... [↗](#)

9. V katerih aminokislinskih ostankih (zapiši le interval od kje do kje) se kanonična struktura razlikuje od njene druge izoformne oblike?

Od 151 do 153 in od 165 do 189.

Function | Entry | Variant viewer | Feature viewer | Genomic coordinates | Publications | External links | History

P01116-1
This isoform has been chosen as the **canonical** sequence. All positional information in this entry refers to it. This is also the sequence that appears in the downloadable versions of the entry.

Name 2A
Synonyms K-Ras4A | 1 Publication | See also sequence in UniParc or sequence clusters in UniRef

Tools | Download | Add | Highlight | Copy sequence

Length 189 | Last updated 1986-07-21 v1
Mass (Da) 21,656 | MD5 Checksum 4A8C310887927CECC35B9DE4B784596E

MTEYKLVVVG¹⁹ AGGVGKLSALT²⁸ IQLIQNHFVD³⁸ EYDPTIEDSY⁴⁸ RKQVVIDG⁵⁸ CLLDILD⁶⁸ TAG⁷⁸ QEEYSAMRDQ⁸⁸ YMRTGEGFLC⁹⁸ VFAINNTKSF¹⁰⁸ EDIH¹¹⁸HYRE¹²⁸QI¹³⁸ KRVK¹⁴⁸DSE¹⁵⁸DV¹⁶⁸P

MVLVGNKCDL¹²⁰ PSRTVDTKQA¹³⁰ QDLAR¹⁴⁰SYGIP¹⁵⁰ FIETSAKTRQ¹⁶⁰ RVEDAFYTLV¹⁷⁰ REIRQYRLKK¹⁸⁰ ISKEEKT¹⁹⁰PGC²⁰⁰ VKIKKCIIM

P01116-2
Name 2B
Synonyms K-Ras4B
See also sequence in UniParc or sequence clusters in UniRef

Differences from canonical
151-153: RVE -> GVD | 5 Publications
165-189: QYRLKKISKEETPGCVKIKKCIIM -> KHKEKMSKDGKKKKKSKTKCVIM | 5 Publications

Show sequence

Primerjava KRAS z drugimi proteini z RAS domeno

1. Poišči več KRAS proteinov iz drugih organizmov in ugotovi, kateri konec proteina (N- ali C-končni del) je evolucijsko bolj ohranjen (omejite se na zbirko Swiss-Prot).

Bolj je ohranjen N-končni del proteina (poravnava narejena s ClustalOmega).

Tool Output | Alignments | Guide Tree | Phylogenetic Tree | Results Viewers | Result Files | Submission Details

Nightingale

COLOR SCHEME: clustal2

LEGEND: A R N D C Q E G H I L K M F P S T W Y V B X Z

9 sequences

HUMAN
MOUSE
RAT
FROG
OPOSSUM
TURKEY
RICE_FISH
MANG_KILLIFISH
CARP

If you use this service, please consider citing the following publication: [The EMBL-EBI Job Dispatcher sequence analysis tools framework in 2024](#). More information about this bioinformatics application can be found in its [bio.tools](#) record.

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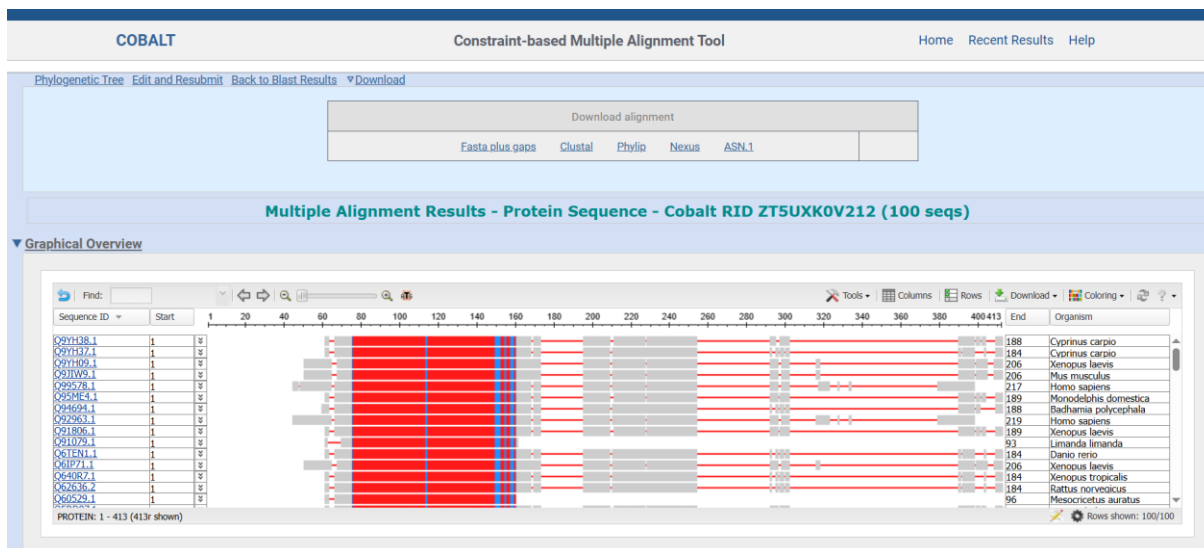
2. Na podlagi KRAS proteinov iz izbranih organizmov prikaži filogenetsko drevo, tako da je človeški KRAS protein na 'začetku/izvoru drevesa'.



3. Protein KRAS vsebuje RAS (GTPazno) domeno, ki je ključna za vezavo GTP/GDP in s tem za uravnavanje njegove aktivnosti v signalnih poteh. Identificiraj proteine (vsaj 15), ki prav tako vsebujejo tako RAS domeno (lahko iz poljubnih organizmov) in s primerjavo teh proteinov med seboj oceni ohranjenost vezavnih mest znotraj RAS družine. Ohranjenost aminokislinskih ostankov prikaži tudi s Sequence Logo-m.

S pomočjo pblast identifikacija proteinov, ki vsebujejo tako RAS domeno kot jo ima protein KRAS. Sledi poravnava zadetkov z orodjem Cobalt in izbira (vsaj 15) proteinov, ki jih prek accession code odpreš v UniProtu. Tam jih shraniš v košarico in jih poravnas. Na človeškem proteinu KRAS (P01116) označiš 'binding site' in ga primerjaš z ostalimi proteini.

Iz poravnave je razvidno, da so vezavna mesta med proteini z RAS domeno vsaj delno ohranjena, nekatera sicer bolj (116-119 aminokislinskega ostanka), druga manj (29-35).



Accession	Description	Links
P01116.1	RecName: Full=GTase KRas; AltName: Full=K-Ras 2; AltName: Full=K-Ras; AltName: Full=c-K-ras; AltName: Full=c-Ki-ras; Contains: RecName: Full=GTase KRas, N-terminally process	Related Information
P08644.3	RecName: Full=GTase KRas; AltName: Full=K-Ras 2; AltName: Full=K-Ras; AltName: Full=c-K-ras; Contains: RecName: Full=GTase KRas, N-terminally process	Related Information
P01117.1	RecName: Full=GTase KRas; AltName: Full=K-Ras; AltName: Full=K-Ras; AltName: Full=c-K-ras; Contains: RecName: Full=GTase KRas, N-terminally process	Related Information
P05774.1	RecName: Full=K-Ras-like protein [Carassius auratus]	Related Information
P23175.1	RecName: Full=GTase HRas; AltName: Full=Transforming protein p21/H-Ras; Flags: Precursor [NS.C58 murine sarcoma virus]	Related Information
P01113.1	RecName: Full=GTase HRas; AltName: Full=Transforming protein p21/H-Ras; Flags: Precursor [Moloney murine sarcoma virus]	Related Information
P01115.1	RecName: Full=Transforming protein p29; Contains: RecName: Full=Transforming protein p21; Flags: Precursor [Harvey murine sarcoma virus]	Related Information
P01114.1	RecName: Full=Transforming protein p29; Contains: RecName: Full=Transforming protein p21; Flags: Precursor [Rasheed rat sarcoma virus]	Related Information
P08642.1	RecName: Full=GTase HRas; AltName: Full=H-Ras-1; AltName: Full=Transforming protein p21; AltName: Full=c-H-ras; AltName: Full=p21ras; Contains: RecName: Full=GTase HRas, N	Related Information
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Q91806.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Xenopus laevis]	Related Information
Q5F352.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Gallus gallus]	Related Information
Q04970.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Rattus norvegicus]	Related Information
P12825.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Cavia porcellus]	Related Information
P01111.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Homo sapiens]	Related Information
P01112.1	RecName: Full=GTase HRas; AltName: Full=H-Ras-1; AltName: Full=H-Ras; AltName: Full=Transforming protein p21; AltName: Full=c-H-ras; AltName: Full=p21ras; Contains: RecName	Related Information
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Q95ME4.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; Flags: Precursor [Monodelphis domestica]	Related Information
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Q42277.1	RecName: Full=GTase KRas; AltName: Full=K-Ras; Short=K-ras; Flags: Precursor [Oryzias latipes]	Related Information
Q02983.1	RecName: Full=GTase KRas; AltName: Full=K-Ras 2; AltName: Full=K-Ras; AltName: Full=c-K-ras; AltName: Full=c-Ki-ras; Contains: RecName: Full=GTase KRas, N-terminally process	Related Information
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Q5EFX7.1	RecName: Full=GTase KRas; AltName: Full=K-Ras; Short=K-ras; Flags: Precursor [Kryptolebias marmoratus]	Related Information
P79737.1	RecName: Full=GTase NRas; AltName: Full=Transforming protein N-Ras; AltName: Full=Z-Ras-B1; Flags: Precursor [Danio rerio]	Related Information
P18262.1	RecName: Full=Ras-like protein; Flags: Precursor [Artemia salina]	Related Information
B4JFJ8.1	RecName: Full=Ras-like protein 1; Flags: Precursor [Drosophila grimshawi]	Related Information
B4NJ72.1	RecName: Full=Ras-like protein 1; Flags: Precursor [Drosophila willistonii]	Related Information
B4I V70.1	RecName: Full=Ras-like protein 1; Flags: Precursor [Drosophila virilis]	Related Information

Overview Trees Percent Identity Matrix Text Output Input Parameters API Request

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<input type="checkbox"/> sp Q5F352 RASN_CHICK	---	MTEYKLVVV	GAGGVGKSA	LT	IQLIQNH	FVDEYDPT	I	EDSYRKQVVI	DGETC	51
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P01116:Binding site

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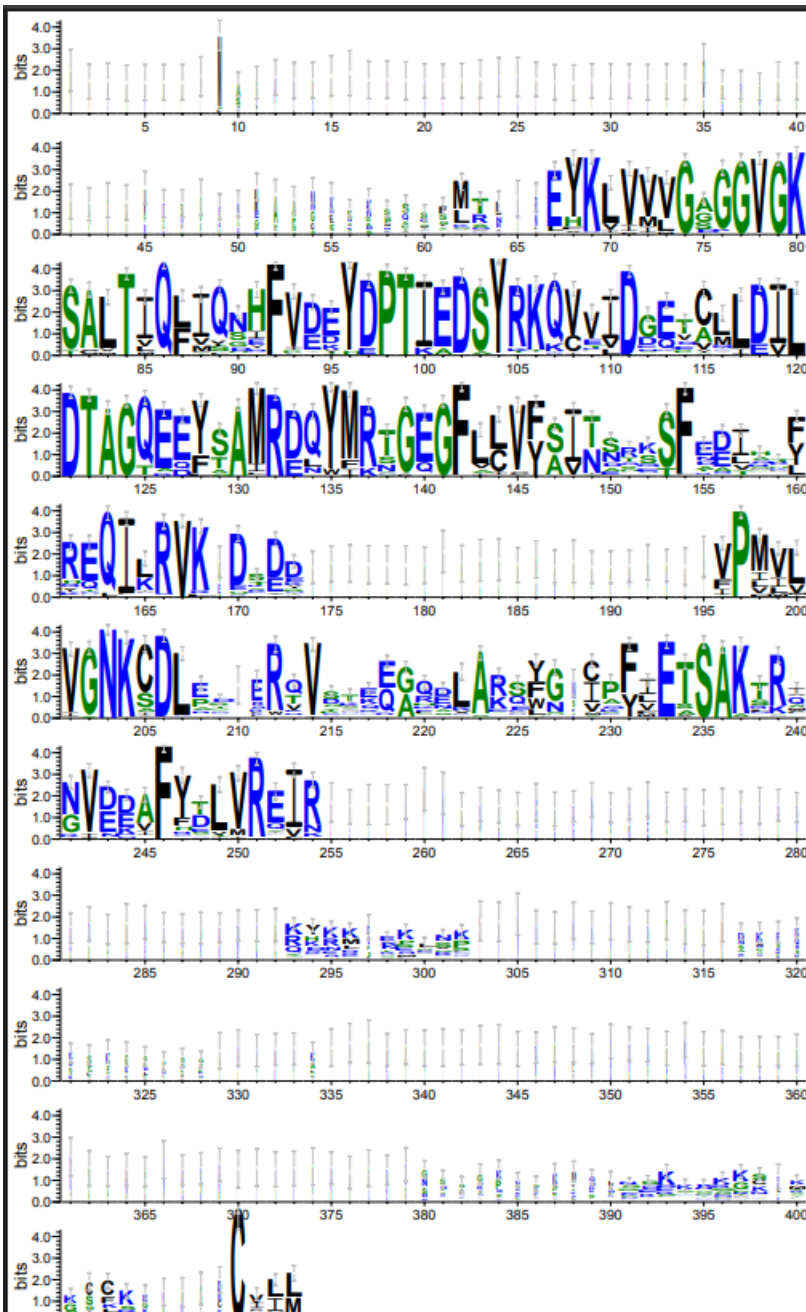
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P01116:Binding site

<input type="checkbox"/> sp Q91806 RASN_XENLA	H	Q	Y	R	M	K	L	D	S	S	E	D	N	N	Q	G	C	I	R	I	P	C	K	L	M	189
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<input type="checkbox"/> sp P08642 RASH_CHICK	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	I	S	189
<input type="checkbox"/> sp P01114 RASH_RRASV	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	L	S	248
<input type="checkbox"/> sp P01115 RASH_MSVAH	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	L	S	241
<input type="checkbox"/> sp P01113 RASH_MSVMO	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	L	S	189
<input type="checkbox"/> sp P23175 RASH_MSUNS	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	L	S	189
<input type="checkbox"/> sp P01112 RASH_HUMAN	R	Q	H	K	L	R	K	L	N	P	P	D	E	S	G	P	G	C	M	S	C	K	V	L	S	189
<input type="checkbox"/> sp P79800 RASK_MELGA	R	K	H	K	E	K	-	M	S	K	D	G	K	K	K	K	K	T	K	T	K	C	I	I	M	188
<input type="checkbox"/> sp P05774 RAS_CARAU	R	Q	Y	R	L	R	K	L	S	K	E	E	E	T	T	Q	C	I	K	L	-	-	-	-	183	
<input type="checkbox"/> sp P01117 RASK_MSVKI	R	Q	Y	R	L	K	I	S	K	E	E	K	T	P	G	C	V	K	I	K	K	C	V	I	M	189
<input type="checkbox"/> sp P01116 RASK_HUMAN	R	Q	Y	R	L	K	I	S	K	E	E	K	T	P	G	C	V	K	I	K	K	C	V	I	M	189
<input type="checkbox"/> sp P08644 RASK_RAT	R	Q	Y	R	L	K	I	S	K	E	E	K	T	P	G	C	V	K	I	K	K	C	V	I	M	189



4. V zbirki Swiss-Prot zdaj poišči človeške proteine, ki vsebujejo RAS domeno (vsaj 10 takih proteinov). Glede na najdene proteine oceni selektivnost zdravila PROTAC za tarčenje KRAS v človeških celicah in možnost potencialne razgradnje napačnih proteinov.

Postopek je podoben kot pri prejšnji nalogi, le da zdaj pri iskanju z blastp pod organizem vpišes človeka, s čimer se omejiš le na iskanje človeških proteinov. Iz poravnave je vidno, da je vezavno mesto, ki ga tvorita 59 in 60 aminokislinski ostanek v človeškem KRAS, ohranjeno pri vseh izbranih človeških proteinih z RAS domeno. Zelo dobro so ohranjeni tudi aminokislinski ostanki od 10 do 18 (številčenje po človeškem KRAS). Ohranjeni so tudi ostanki od 116 do 119, z izjemo cisteina na 118 mestu. Ostanki 29-35 so najslabše ohranjeni.

Prisotnost določenih ohranjenih sekvenc ostankov dopušča možnost vezave PROTAC na napačno tarčo in tako razgradnjo napačnih proteinov. Potrebno pa je imeti v mislih, da je tudi pomembno, kateri aminokislinski ostanek manjka. Če manjka npr. cistein, ki je zaradi svoje nukleofilnosti pogosto za vezavo ključnega pomena, je vendarle drugače, kot če manjka ostanek, ki za vezavo nima ključnega pomena (npr. običajno glicin).

Overview	Trees	Percent Identity Matrix	Text Output	Input Parameters	API Request													
<input type="checkbox"/> sp P11233 RALA_HUMAN		-----MAANKPKQNSLALHKVIMV	GS	GGV	GKS	AL	T	L	Q	F	M	Y	D	E	F	V	40	
<input type="checkbox"/> sp P11234 RALB_HUMAN		-----MAANKSKGQSSLALHKVIMV	GS	GGV	GKS	AL	T	L	Q	F	M	Y	D	E	F	V	40	
<input type="checkbox"/> sp Q92963 RIT1_HUMAN		MDSG-----TRPVGSC-CSSPAGLSREYKLVML	GAG	GGV	GKS	AM	T	M	Q	F	I	S	H	R	F	P	46	
<input type="checkbox"/> sp Q99578 RIT2_HUMAN		ME-----VENEASCSPGSAAGSREYKVVML	GAG	GGV	GKS	AM	T	M	Q	F	I	S	H	Q	F	P	47	
<input type="checkbox"/> sp Q9Y3L5 RAP2C_HUMAN		-----MREYKVVVL	GS	GGV	GKS	AL	T	V	Q	F	V	T	G	T	F	I	29	
<input type="checkbox"/> sp P62834 RAP1A_HUMAN		-----MREYKLVVL	GS	GGV	GKS	AL	T	V	Q	F	V	G	G	I	F	V	29	
<input type="checkbox"/> sp P61224 RAP1B_HUMAN		-----MREYKLVVL	GS	GGV	GKS	AL	T	V	Q	F	V	Q	G	I	F	V	29	
<input type="checkbox"/> sp A6NIZ1 RP1BL_HUMAN		-----MREYKLVVL	GS	R	GGV	GKS	AL	T	V	Q	F	V	G	G	I	F	V	29
<input type="checkbox"/> sp P01116 RASK_HUMAN		-----MTEYKLVVV	GAG	GGV	GKS	AL	T	I	Q	L	I	Q	N	H	F	V	29	
<input type="checkbox"/> sp P01111 RASN_HUMAN		-----MTEYKLVVV	GAG	GGV	GKS	AL	T	I	Q	L	I	Q	N	H	F	V	29	
<input type="checkbox"/> sp P01112 RASH_HUMAN		-----MTEYKLVVV	GAG	GGV	GKS	AL	T	I	Q	L	I	Q	N	H	F	V	29	
<input type="checkbox"/> sp O14807 RASM_HUMAN		-----MATSAPVSDNLPYKLVVV	G	D	GGV	GKS	AL	T	I	Q	F	Q	K	I	F	V	39	
<input type="checkbox"/> sp P62070 RRAS2_HUMAN		-----MAAAGWRDGSQEKYRLVVV	GGG	GGV	GKS	AL	T	I	Q	F	I	Q	S	Y	F	V	40	
<input type="checkbox"/> sp P10301 RRAS_HUMAN		MSSGAASGTGRGRPRGGPGPGDPPPSETHKLVVV	GGG	GGV	GKS	AL	T	I	Q	F	I	Q	S	Y	F	V	55	

P01116:Binding site

<input type="checkbox"/> sp P11233 RALA_HUMAN	EDYEP	KADSYRKKVVL	DGEEVQID	LD	TAGQ	EDYAA	IRDNY	FRS	GE	GF	LCV	FSI	95
<input type="checkbox"/> sp P11234 RALB_HUMAN	EDYEP	KADSYRKKVVL	DGEEVQID	LD	TAGQ	EDYAA	IRDNY	FRS	GE	GF	LLV	FSI	95
<input type="checkbox"/> sp Q92963 RIT1_HUMAN	EDHDPT	IEDAYKIRIRI	DDEPANLD	LD	TAGQ	AEFTAMR	DQYMR	AGE	GF	I	ICYSI	102	
<input type="checkbox"/> sp Q99578 RIT2_HUMAN	DYHDPT	IEDAYKIQVR	IDNEPAILD	LD	TAGQ	AEFTAMR	EYMRG	GEGF	I	ICYSV	101		
<input type="checkbox"/> sp Q9Y3L5 RAP2C_HUMAN	EKYDPT	IEDFYRKEIEVD	SSPSVLEI	LD	TAGT	EQFASMR	LDY	IKNG	QGF	ILV	VYSL	84	
<input type="checkbox"/> sp P62834 RAP1A_HUMAN	EKYDPT	IEDSYRKQVEV	DCCQCML	LD	TAGT	EQFTAMR	LDY	MKNG	QGF	ALV	VYSI	84	
<input type="checkbox"/> sp P61224 RAP1B_HUMAN	EKYDPT	IEDSYRKQVEV	DAQQCML	LD	TAGT	EQFTAMR	LDY	MKNG	QGF	ALV	VYSI	84	
<input type="checkbox"/> sp A6NIZ1 RP1BL_HUMAN	EKYDPT	IEDSYRQVEV	DAQQCML	LD	TAGT	EQFTAMR	LDY	MKNG	QGF	ALV	VYSI	84	
<input type="checkbox"/> sp P01116 RASK_HUMAN	DEYDPT	IEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84	
<input type="checkbox"/> sp P01111 RASN_HUMAN	DEYDPT	IEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84	
<input type="checkbox"/> sp P01112 RASH_HUMAN	DEYDPT	IEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84	

Overview	Trees	Percent Identity Matrix	Text Output	Input Parameters	API Request							
<input type="checkbox"/> sp Q9Y3L5 RAP2C_HUMAN		EKYDPTIEDFYRKEIEVDSSPSVLEI	LD	TAGT	EQFASMRDLY	IKNG	QGF	ILV	VYSL	84		
<input type="checkbox"/> sp P62834 RAP1A_HUMAN		EKYDPTIEDSYRKQVEVDCCQCML	LD	TAGT	EQFTAMRDL	YMKNG	QGF	ALV	VYSI	84		
<input type="checkbox"/> sp P61224 RAP1B_HUMAN		EKYDPTIEDSYRKQVEVDCCQCML	LD	TAGT	EQFTAMRDL	YMKNG	QGF	ALV	VYSI	84		
<input type="checkbox"/> sp A6NIZ1 RP1BL_HUMAN		EKYDPTIEDSYRQVEVDCCQCML	LD	TAGT	EQFTAMRDL	YMKNG	QGF	ALV	VYSI	84		
<input type="checkbox"/> sp P01116 RASK_HUMAN		DEYDPTIEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84
<input type="checkbox"/> sp P01111 RASN_HUMAN		DEYDPTIEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84
<input type="checkbox"/> sp P01112 RASH_HUMAN		DEYDPTIEDSYRKQVV	DGETCLLD	LD	TAGQ	EEYSAMR	DQYMR	TGEG	FL	CV	FAI	84
<input type="checkbox"/> sp O14807 RASM_HUMAN		PDYDPTIEDSYLKHTEDNQWAL	LDVLD	LD	TAGQ	EEFSAMR	EQYMR	TGEG	FL	IV	YSV	94
<input type="checkbox"/> sp P62070 RRAS2_HUMAN		TDYDPTIEDSYTKQCV	LDRAARLD	LD	TAGQ	EEFGAMR	EQYMR	TGEG	FL	LV	FSV	95
<input type="checkbox"/> sp P10301 RRAS_HUMAN		SDYDPTIEDSYTKICSV	DGIPARLD	LD	TAGQ	EEFGAMR	EQYMR	AGHG	FL	LV	FAI	110

P01116:Binding site

<input type="checkbox"/> sp P11233 RALA_HUMAN	T	E	M	E	S	F	A	A	T	A	D	F	R	E	Q	L	R	V	K	E	D	-	E	N	V	F	L	L	V	G	N	K	S	D	L	E	D	K	R	Q	V	S	V	E	E	A	K	N	R	A	E	Q	W	149		
<input type="checkbox"/> sp P11234 RALB_HUMAN	T	E	H	E	S	F	T	A	T	A	E	F	R	E	Q	L	R	V	K	A	E	E	D	K	I	P	L	L	V	G	N	K	S	D	L	E	E	R	R	Q	V	P	E	E	A	R	S	K	A	E	E	W	150			
<input type="checkbox"/> sp Q92963 RIT1_HUMAN	T	D	R	R	S	F	H	E	V	R	F	K	Q	L	I	Y	R	V	R	T	-	D	E	T	P	V	L	V	G	N	K	S	D	L	K	L	R	Q	V	T	K	E	E	G	L	A	R	E	F	156						
<input type="checkbox"/> sp Q99578 RIT2_HUMAN	T	D	R	Q	S	F	Q	E	A	A	K	F	K	E	L	I	F	Q	V	R	H	-	Y	E	I	P	L	V	L	V	G	N	K	I	D	L	E	Q	F	R	Q	V	S	T	E	E	G	L	S	L	A	Q	E	Y	155	
<input type="checkbox"/> sp Q9Y3L5 RAP2C_HUMAN	V	N	Q	Q	S	F	Q	D	I	K	P	M	R	D	I	V	R	V	K	R	Y	-	E	K	V	L	I	L	V	G	N	K	V	D	L	E	P	E	R	E	V	M	S	E	G	R	A	L	A	Q	E	W	138			
<input type="checkbox"/> sp P62834 RAP1A_HUMAN	T	A	Q	S	T	F	N	D	L	Q	D	L	R	E	Q	L	R	V	K	D	T	-	E	D	V	P	M	I	L	V	G	N	K	C	D	L	E	D	E	R	V	G	K	E	Q	Q	N	L	A	R	Q	W	138			
<input type="checkbox"/> sp P61224 RAP1B_HUMAN	T	A	Q	S	T	F	N	D	L	Q	D	L	R	E	Q	L	R	V	K	D	T	-	D	D	V	P	M	I	L	V	G	N	K	C	D	L	E	D	E	R	V	G	K	E	Q	Q	N	L	A	R	Q	W	138			
<input type="checkbox"/> sp A6NIZ1 RP1BL_HUMAN	T	A	Q	S	T	F	N	D	L	Q	D	L	R	E	Q	L	R	V	K	D	T	-	D	D	V	P	M	I	L	V	G	N	K	C	D	L	E	D	E	R	V	G	K	E	Q	Q	N	L	A	R	Q	W	138			
<input type="checkbox"/> sp P01116 RASK_HUMAN	N	N	T	K	S	F	E	D	I	H	Q	Y	R	E	Q	I	K	R	V	K	D	S	-	E	D	V	P	M	V	L	V	G	N	K	C	D	L	P	S	-	R	T	V	D	T	K	Q	A	Q	D	L	A	R	S	Y	137
<input type="checkbox"/> sp P01111 RASN_HUMAN	N	N	S	K	S	F	A	D	I	N	L	Y	R	E	Q	I	K	R	V	K	D	S	-	D	D	V	P	M	V	L	V	G	N	K	C	D	L	P	T	-	R	T	V	D	T	K	Q	A	H	E	L	A	K	S	Y	137
<input type="checkbox"/> sp P01112 RASH_HUMAN	N	N	T	K	S	F	E	D	I	H	Q	Y	R	E	Q	I	K	R	V	K	D	S	-	D	D	V	P	M	V	L	V	G	N	K	C	D	L	A	A	-	R	T	V	E	S	R	Q	A	D	L	A	R	S	Y	137	
<input type="checkbox"/> sp O14807 RASM_HUMAN	N	D	T	K	A	S	F	E	H	V	D	R	F	H	Q	L	I	R	V	K	D	R	-	E	S	F	P	M	I	L	V	N	K	V	D	L	M	H	L	R	K	I	T	R	E	Q	G	K	E	M	A	T	K	H	148	
<input type="checkbox"/> sp P62070 RRAS2_HUMAN	T	D	R	G	S	F	E	E	I	Y	K	F	Q	R	I	L	R	V	K	D	R	-	D	E	F	P	M	I	L	I	G	N	K	A	D	L	D	H	Q	R	Q	V	T	Q	E	E	G	Q	L	A	R	Q	L	149		
<input type="checkbox"/> sp P10301 RRAS_HUMAN	N	D	R	Q	S	F	N	E	V	G	K	L	F	T	Q	I	L	R	V	K	D	R	-	D	D	F	P	V	L	V	L	V	G	N	K	A	D	L	E	S	Q	R	V	P	R	S	E	A	S	A	F	G	A	S	H	164

Overview	Trees	Percent Identity Matrix	Text Output	Input Parameters	API Request
<input type="checkbox"/>	sp P11233 RALA_HUMAN	- NVNYVETSAK - TRANVDKVFDFLMRE	I RARKMEDSKEKNGKKKRK - - - - SLAK		197
<input type="checkbox"/>	sp P11234 RALB_HUMAN	- GVQYVETSAK - TRANVDKVFDFLMRE	I RTKKMSENKDKNGKKSSK - - - - N-KK		197
<input type="checkbox"/>	sp Q92963 RIT1_HUMAN	- SCPFETSAAYRYYIDDVFHALVRE	I RRKEKEAVLAMEKKSPPKNSVWKRLKS		209
<input type="checkbox"/>	sp Q99578 RIT2_HUMAN	- NCGFETSAALRFCIDDAFHGLVRE	I RKKESMPS-LMEKKLKRKDSLWKLLKG		207
<input type="checkbox"/>	sp Q9Y3L5 RAP2C_HUMAN	- GCPFMETSAK-SKSMVDELFAEIVRQ	MNYSSLPEK - - - - -		172
<input type="checkbox"/>	sp P62834 RAP1A_HUMAN	CNCAFLLESSAK-SKINVNEIFYDLVRQ	I NRKTPVEK - - - - -		173
<input type="checkbox"/>	sp P61224 RAP1B_HUMAN	NNCAFLLESSAK-SKINVNEIFYDLVRQ	I NRKTPVPG - - - - -		173
<input type="checkbox"/>	sp A6NIZ1 RP1BL_HUMAN	NNCAFLLESSAK-SKINVNEIFYDLVRQ	I NRKTPVPG - - - - -		173
<input type="checkbox"/>	sp P01116 RASK_HUMAN	- GIPFIETSAK-TRQRVEDAFYTLVRE	I RQYRLKKISKE - - - - - EKTPG - - - -		179
<input type="checkbox"/>	sp P01111 RASN_HUMAN	- GIPFIETSAK-TRQGVEDAFYTLVRE	I RQYRMKKLNSS - - - - - DDGTQG - - - -		180
<input type="checkbox"/>	sp P01112 RASH_HUMAN	- GIPYIETSAK-TRQGVEDAFYTLVRE	I RQHKLRLKNPP - - - - - DESGPG - - - -		180
<input type="checkbox"/>	sp O14807 RASM_HUMAN	- NIPYIETSAKDPPLNVDFHDLVRV	I RQQIPEKSKPK - - - - - KKKTKWRGDR - -		196
<input type="checkbox"/>	sp P62070 RRAS2_HUMAN	- KVTYMEASAK-IRMNVDQAFHELVRV	I RKFQEQCSPS - - - - - PEPTRK - - - -		192
<input type="checkbox"/>	sp P10301 RRAS_HUMAN	- HVAYFEASAK-LRLNVDEAFELVRAV	I RKYQEQLPPS - - - - - PPSAP - - - -		206

P01116:Binding site

<input type="checkbox"/>	sp P11233 RALA_HUMAN	RI - - - - RERCCIL -		206
<input type="checkbox"/>	sp P11234 RALB_HUMAN	SF - - - - KERCCLL -		206
<input type="checkbox"/>	sp Q92963 RIT1_HUMAN	PFRKKKDSVT - - - -		219
<input type="checkbox"/>	sp Q99578 RIT2_HUMAN	SLKKKRENMT - - - -		217
<input type="checkbox"/>	sp Q9Y3L5 RAP2C_HUMAN	- - - - QDQCCTTCVVQ		183
<input type="checkbox"/>	sp P62834 RAP1A_HUMAN	- - - - KKPKKKSCLLL		184
<input type="checkbox"/>	sp P61224 RAP1B_HUMAN	- - - - KARKKSSCQLL		184
<input type="checkbox"/>	sp A6NIZ1 RP1BL_HUMAN	- - - - KARKKSSCQLL		184
<input type="checkbox"/>	sp P01116 RASK_HUMAN	- - - - CVKIKKCIIM		189
<input type="checkbox"/>	sp P01111 RASN_HUMAN	- - - - CMGLP-CVVM		189
<input type="checkbox"/>	sp P01112 RASH_HUMAN	- - - - CMSCK-CVLS		189

Primerjava KRAS z drugimi PROTAC tarčami

Poleg proteina KRAS so pomembne tarče za razvoj PROTAC terapij tudi BET proteini, med katerimi je posebej pomemben BRD4 (bromodomain containing 4).

1. Kako dolga je mRNA, ki kodira človeški protein BRD4 (glej varianto transkripta 3)?

3234 bp

Nucleotide Help

Advanced

GenBank Send to: Change region shown

Homo sapiens bromodomain containing 4 (BRD4), transcript variant 3, mRNA

NCBI Reference Sequence: NM_001330384.2
[FASTA](#) [Graphics](#)

Go to:

<p>LOCUS NM_001330384 3234 bp mRNA linear PRI 03-FEB-2026</p> <p>DEFINITION Homo sapiens bromodomain containing 4 (BRD4), transcript variant 3, mRNA.</p> <p>ACCESSION NM_001330384 XM_011527855</p> <p>VERSION NM_001330384.2</p> <p>KEYWORDS RefSeq.</p> <p>SOURCE Homo sapiens (human)</p> <p>ORGANISM Homo sapiens</p> <p>Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.</p> <p>REFERENCE 1 (bases 1 to 3234)</p> <p>AUTHORS Yang,Y.H., Yan,F., Yuan,W., Shi,P.S., Wu,S.M. and Cui,D.J.</p> <p>TITLE High-altitude hypoxia promotes BRD4-mediated activation of the Wnt/beta-catenin pathway and disruption of intestinal barrier</p> <p>JOURNAL Cell Signal 120, 111187 (2024)</p> <p>PUBMED 38648894</p> <p>REMARK GeneRIF: High-altitude hypoxia promotes BRD4-mediated activation of the Wnt/beta-catenin pathway and disruption of intestinal barrier.</p> <p>REFERENCE 2 (bases 1 to 3234)</p> <p>AUTHORS Chen,F., Li,S., Liu,M., Qian,C., Shang,Z., Song,X., Jiang,W. and Tu,C.</p> <p>TITLE Targeting BRD4 mitigates hepatocellular lipotoxicity by suppressing the NLRP3 inflammasome activation and GSDMD-mediated hepatocyte pyroptosis</p> <p>JOURNAL Cell Mol Life Sci 81 (1), 295 (2024)</p>	<p>Reference sequence information</p> <p>RefSeq alternative splicing See 15 reference mRNA sequence splice variants for the BRD4 gene.</p> <p>More about the BRD4 gene</p> <p>The protein encoded by this gene is homologous to the murine protein MCAP, which associates with chromosomes during mitosis, and to the huma...</p> <p>Also Known As: CAP, CDLS6, FSHRG4, HUN...</p> <p>Related information</p> <p>Protein</p>
--	---

2. Koliko eksonov vsebuje njegova mRNA (glej varianto transkripta 3)?

Informacijo najdeš v zgornjem zadetku pod razdelkom Features, kjer prešteješ eksoni. Vseh eksonov je 12.

Ker se PROTAC molekula na tarčni protein veže preko liganda, ki prepozna specifično vezavno mesto na proteinu, dostopnost in struktura teh mest pomembno vplivata na uspešnost degradacije proteina. Zato primerjajte proteina KRAS in BRD4 ter ocenite, kateri predstavlja primernejšo tarčo za razvoj PROTAC terapij glede na dostopnost in definiranost vezavnih mest za ligand.

* V AlphaFold Protein Structure Database poiščite strukturi obeh proteinov (povezavi najdete v UniProt).

* Pri iskanju modela strukture proteina KRAS boš našel dva modela, za protein BRD4 pa tri modele. Za KRAS uporabi oba modela in zanj v Chimeri X naredi superpozicijo, za BRD4 pa le prvi model. S pomočjo UniProt-a ustrezno identificiraj vezavna mesta obeh proteinov in jih v ChimeriX označi z drugo barvo.

KRAS

AlphaFold Protein Structure Database

Home About FAQs Downloads API Collaborators

P01116

Examples: MENFOKVEKIGEGTYGV... Free fatty acid receptor 2 At1g58602 Q911F6 E. coli See search help Go to online course

Showing all search results for P01116

1 - 2 of 2 results

Filter by: Download data

Entry type
Monomers (2)

Status

Review Reviewed (Swiss-Prot) (2)

GTPase KRas

Monomer • AF-P01116-2-F1-v6 • Google DeepMind dataset

Protein	GTPase KRas
Gene	KRAS
Source organism	<i>Homo sapiens</i> search this organism
UniProt	P01116-2 go to UniProt
Experimental structures	487 PDB structures for P01116-2 go to PDB-KR

BRD4

Search for protein, gene, UniProt accession or organism or sequence search

Examples: MENFOKVEKIGEGTYGV... Free fatty acid receptor 2 At1g58602 Q911F6 E. coli See search help Go to online course

Showing all search results for O60885

1 - 3 of 3 results

Filter by: Download data

Entry type
Monomers (3)

Status

Review Reviewed (Swiss-Prot) (3)

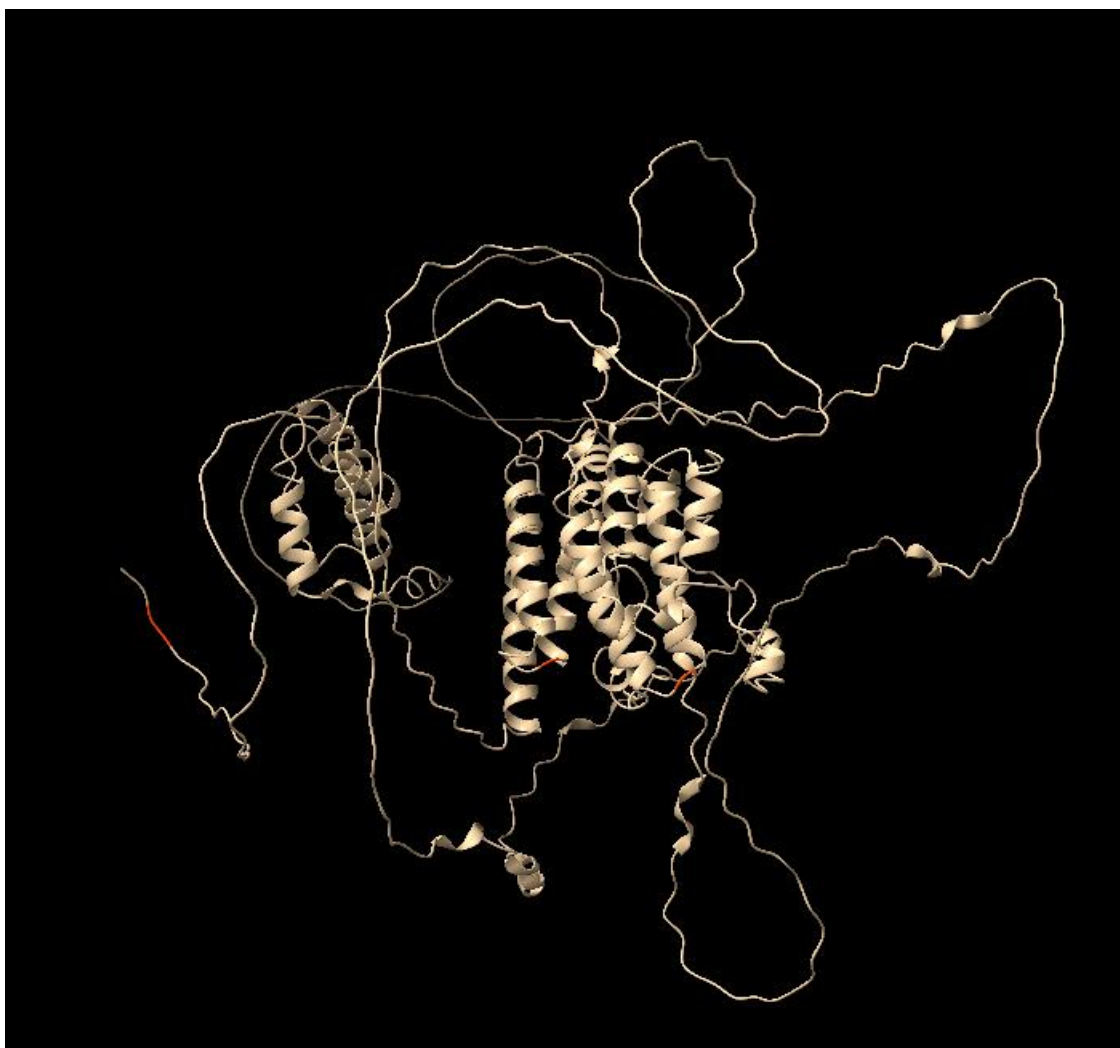
Show predictions for sequences found only in UniProt reference

Bromodomain-containing protein 4

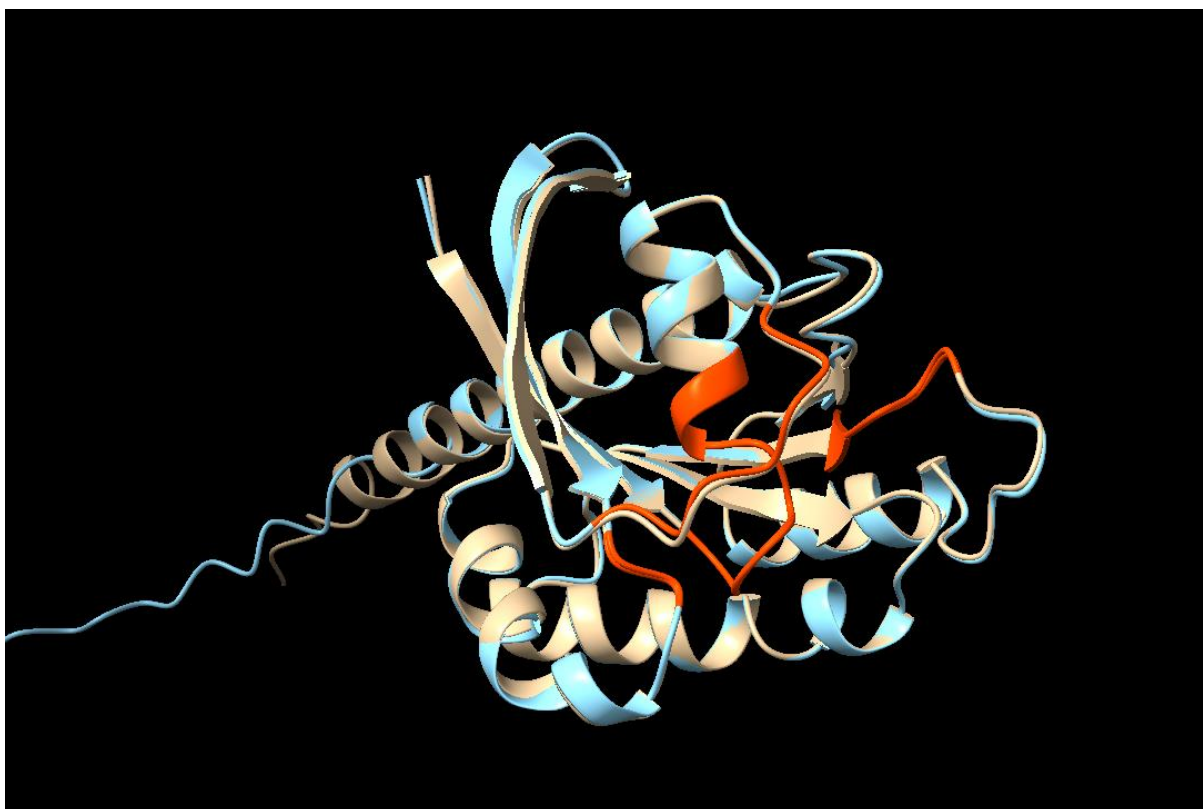
Monomer • AF-O60885-2-F1-v6 • Google DeepMind dataset

Protein	Bromodomain-containing protein 4
Gene	BRD4
Source organism	<i>Homo sapiens</i> search this organism
UniProt	O60885-2 go to UniProt
Experimental structures	618 PDB structures for O60885-2 go to PDB-KB
Global quality	average pLDDT 66 (Low)
Sequence length	722

ChimeraX – BRD4



ChimeraX – KRAS



1. Na podlagi primerjave same definiranosti vezavnih mest in možnosti selektivne vezave liganda, predvidi, kateri protein predstavlja primernejšo PROTAC tarčo. Pomagaš si lahko tudi z UniProt-om (preveri domene BRD4).

Protein KRAS ima plitve in dinamične interakcijske površine ter slabo definirana vezavna mesta za vezavo ligandov, zaradi česar predstavlja zahtevno tarčo PROTAC terapij. Nasprotno protein BRD4 vsebuje dobro definirane bromodomene (podatek v UniProtu pod Family and Domains), sama vezava ligandov na BRD4 pa je bolj specifična in stabilna, zaradi česar slednji predstavlja primernejšo PROTAC tarčo.