

Uniprot Activity 2

- What is the function of Src tyrosine kinases?

As name already hints at, it is a tyrosine kinase, so it transfers P_i to tyrosine residues and thereby activating the latter protein. It is situated in the membrane of the cell and plays a crucial role in the growth signaling pathway. (Therefore also for cancer)

- Is there only one Src tyrosine kinase? What are some others?

Only one **Src** tyrosine kinase, but a large variety of very similar tyrosine kinases. (which can even compensate for experimental src knock-out!)

- What is special about v-Src? How does it differ from c-Src?

viral-Src is a protein that resembles the “normal cellular-Src”. The problem is, that v-Src is constitutively active and as a consequence also growth signaling, which leads to cancer formation over time...

- What is the purpose of most drug design studies against Src?

Block constitutively form of src.

Go to the Abl kinase entry in the PDB by clicking on 1opl link in the molecule of the month page or search for the PDB ID 1OPL in PDB.

Clicking on “search on pubmed” will take you to the primary citation link for Abl kinase structure in PUBMED. What is the name of the article?

- Structural basis for the autoinhibition of c-Abl tyrosine kinase.

Now let's examine Src kinase family of proteins .Abl kinase is a Src kinase. Search for reviewed, human Src kinases with Src as the protein family filter.

Filter byⁱ

Reviewed (13)
Swiss-Prot

Popular organisms
Human (13)

Proteomes
UP000005640 (13)

Search terms
Filter "src" as:
protein family

View by
Results table

Taxonomy

Keywords

Gene Ontology

Enzyme class

Pathway

UniRef

Your results in sequence clusters with identity of:
100%, 90% or 50%

Demo

Help video

Entry	Entry name	Protein names	Gene names	Organism	Length	Protein families
P51451	BLK_HUMAN	Tyrosine-protein kinase Blk	BLK	Homo sapiens (Human)	505	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P42685	FRK_HUMAN	Tyrosine-protein kinase FRK	FRK PTK5, RAK	Homo sapiens (Human)	505	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P09769	FGR_HUMAN	Tyrosine-protein kinase Fgr	FGR SRC2	Homo sapiens (Human)	529	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P06241	FYN_HUMAN	Tyrosine-protein kinase Fyn	FYN	Homo sapiens (Human)	537	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P07948	LYN_HUMAN	Tyrosine-protein kinase Lyn	LYN JTK8	Homo sapiens (Human)	512	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P08631	HCK_HUMAN	Tyrosine-protein kinase HCK	HCK	Homo sapiens (Human)	526	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
Q15788	NCOA1_HUMAN	Nuclear receptor coactivator 1	NCOA1 BHLHE74, SRC1	Homo sapiens (Human)	1,441	SRC/p160 nuclear receptor coactivator family
Q9Y6Q9	NCOA3_HUMAN	Nuclear receptor coactivator 3	NCOA3 AIB1, BHLHE42, RAC3, TRAM1	Homo sapiens (Human)	1,424	SRC/p160 nuclear receptor coactivator family
Q15596	NCOA2_HUMAN	Nuclear receptor coactivator 2	NCOA2 BHLHE75, SRC2, TIF2	Homo sapiens (Human)	1,464	SRC/p160 nuclear receptor coactivator family
P06239	LCK_HUMAN	Tyrosine-protein kinase Lck	LCK	Homo sapiens (Human)	509	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P07947	YES_HUMAN	Tyrosine-protein kinase Yes	YES1 YES	Homo sapiens (Human)	543	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
Q9H3Y6	SRMS_HUMAN	Tyrosine-protein kinase Srms	SRMS C20orf148	Homo sapiens (Human)	488	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily
P12931	SRC_HUMAN	Proto-oncogene tyrosine-protein kin...	SRC SRC1	Homo sapiens (Human)	536	Protein kinase superfamily, Tyr protein kinase family, SRC subfamily

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- How many proteins are there?
 - How many human Src kinases? **13**
 - How many Uniref100: **4** (with SRC_Human itself) belonging to cluster with ID UniRef100_P12931
 - Uniref90? **18** (also counting SRC_Human itself) proteins belong to the **cluster with ID: UniRef90_P12931**
 - What are these? Uniref100 combines identical sequences and fragments with 11 or more residues into a single UniRef entry, while UniRef90 in

turn is built from UniRef100 sequences by clustering them so that each cluster itself then has 90% identity within its cluster.

- Select all and align.
- Can you identify any residues/regions that are highly conserved? (hint: motif) (hint: symbols underneath the alignment) (hint: look for a triplet)

In grey

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P12931      SRC HUMAN      161  SERLLLNAEENPRGTFLLVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSSGGFYITSR      220
K7B763      K7B763 PANTR  161  SERLLLNAEENPRGTFLLVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSSGGFYITSR      220
G3QWW0      G3QWW0 GORGO      161  SERLLLNAEENPRGTFLLVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSSGGFYITSR      220
A0A402E9W6  A0A402E9W6 9SAUR      171  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      230
A0A2D4G6D1  A0A2D4G6D1 MICCO      1   -----PENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      53
A0A2J8VJN2  A0A2J8VJN2 PONAB      161  SERLLLNENPRGTFLLVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSSGGFYITSR      220
H9GID5      H9GID5 ANOCA      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
V8PCK4      V8PCK4 OPHHA      165  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      224
UPI0000135F28      160  SERLLLNENPRGTFLLVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSSGGFYITSR      219
UPI00009E2D300      163  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      222
UPI0000462C649      163  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      222
UPI00009E3FC01      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI0000E783033      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI000074FBB2E      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI000109F3D59      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI0000775746F      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI00004418C84      157  SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      216
UPI00009E4579B      76   SERLLLNENPRGTFLLARESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDNGGGFYITSR      135
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P12931      SRC HUMAN      221  TOENSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      280
K7B763      K7B763 PANTR  221  TOENSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      280
G3QWW0      G3QWW0 GORGO      221  TOENSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      280
A0A402E9W6  A0A402E9W6 9SAUR      231  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      290
A0A2D4G6D1  A0A2D4G6D1 MICCO      54  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      113
A0A2J8VJN2  A0A2J8VJN2 PONAB      221  TOENSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      280
H9GID5      H9GID5 ANOCA      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
V8PCK4      V8PCK4 OPHHA      225  TOESSLQQLVAYYYSR-----
UPI0000135F28      220  TOENSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      279
UPI00009E2D300      223  TOESSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      282
UPI0000462C649      223  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      282
UPI00009E3FC01      217  TOESSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI0000E783033      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI000074FBB2E      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI000109F3D59      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI0000775746F      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI00004418C84      217  TOESSLQQLVAYYYSKHDGLCHRLTNVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      276
UPI00009E4579B      136  TOESSLQQLVAYYYSKHDGLCHRLTTVCPTSKPQTQGLAKDAWEIPRESLRLEVKLGQGC      195
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- How conserved is the active site residue (how can you find it)? What is it?

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P12931      SRC HUMAN      337  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      395
K7B763      K7B763 PANTR  337  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      395
G3QWW0      G3QWW0 GORGO      337  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      395
A0A402E9W6  A0A402E9W6 9SAUR      348  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      405
A0A2D4G6D1  A0A2D4G6D1 MICCO      116  -----
A0A2J8VJN2  A0A2J8VJN2 PONAB      337  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      395
H9GID5      H9GID5 ANOCA      334  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
V8PCK4      V8PCK4 OPHHA      293  CEFLTTICSLVGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      352
UPI0000135F28      336  -IYIVTEYMSKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      394
UPI00009E2D300      340  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      397
UPI0000462C649      340  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      397
UPI00009E3FC01      334  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
UPI0000E783033      334  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
UPI000074FBB2E      334  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
UPI000109F3D59      334  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
UPI0000775746F      320  --FLTTFYSTVGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      377
UPI00004418C84      334  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      391
UPI00009E4579B      253  --YIVTEYMCKGSLLDFLKGETGKYLRPLQLVDMAAQIASGMAYVERMNYVHRDLRAANI      310

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In red. It is only one amino acid (D= aspartic acid), thus negative charge. It is conserved across all other cluster-proteins

- Are there any variants around the active site residue?



The red dot at position 389 is the active site. There is a missense R > W variant right next to it (position 388) with probably damaging consequences. The change of the basic positively charged Arginine to a aromatic, neutrally charged Tryptophan could have an impact on the structure of the src kinase and due to its proximity to the active site also on that! On the whole there are other 4 variants within 4 residues.

kinase. For a Uniprot entry, there may be several PDB structures associated with it. Look under the column Positions. Pick the PDB ID with the maximum coverage (coverage refers to fraction of residues for which there is structural data with respect to the whole sequence length).

What is the PDB ID for this structure?

1A07

Visualize the structure within UniProt to obtain a view similar to that in the Abl kinase paper. <https://www.sciencedirect.com/science/article/pii/S0092867403001946?via%3Dihub>

Are there any red dots? What are they? Phosphate Groups

