Research Article

Characterization of rho-associated protein kinase Rock1 by using online bioinformatics tools

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Abstract

Abstract: ROCK-signalling system is involved in regulation of cellular growth, and life cycle through control of muscle cell contractility, change in ROCK pathway and resultant impaired cell contractility cause to disease in different organs, including cardiovascular, respiratory and renal systems. Hence, ROCK inhibitors are potential therapeutic agents for hypertension, heart disease, pulmonary disease, asthma, erectile dysfunction, diabetic renal failure, chronic nephritis and glaucoma. ROCK inhibitors, similar to some other cytoskeletal drugs, could increase matrix metalloproteinase expression in cells and may induce extracellular matrix reorganization, ROCK inhibitors could weaken cell attachment to its extracellular matrix, which results in relaxation of the whole of tissue and hence, it is also probable that ROCK inhibitors enhance outflow through unknown mechanisms. Rho-associated kinase inhibitors relax smooth muscle tone in brain vasculature and could potentially increase optic nerve head perfusion. ROCK inhibitors could have neuroprotective effects on ganglion cells.

Keywords: Molecular functionion Kinase, Serine/threonine-protein kinase, Transferase matrix assembly process, essential for osteoblast mineralization.

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INTRODUCTION

Protein kinase which is a key regulator of actin cytoskeleton and cell polarity. Involved in regulation of smooth muscle contraction, actin cytoskeleton organization, stress fiber and focal adhesion formation, neurite retraction, cell adhesion and motility. Acts as a suppressor of inflammatory cell migration by regulating. Required for centrosome positioning and centrosome-dependent exit from mitosis. Plays a role in terminal erythroid differentiation. May regulate closure of the eyelids and ventral body wall by inducing the assembly of actomyosin bundles. Promotes keratinocyte terminal differentiation. Involved in osteoblast compaction.

Annotation

ROCK1 Gene Structure
Chromosome: chr18
Orientation: -
Length coding sequence: 4062 nucleotides.

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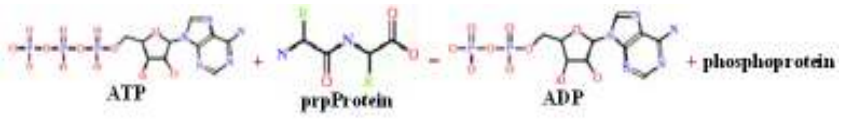
Table 1

Region	Start	End	Region Length	Phase at end
UTR	18,690,872	18,691,812		
Exon	18,690,779	18,690,871	93	0
Exon	18,650,493	18,650,574	82	1
Exon	18,629,741	18,629,841	101	0
Exon	18,629,053	18,629,190	138	0
Exon	18,625,253	18,625,428	176	2
Exon	18,624,063	18,624,147	85	0
Exon	18,622,526	18,622,670	145	1
Exon	18,622,058	18,622,196	139	2
Exon	18,619,433	18,619,524	92	1
Exon	18,608,737	18,608,896	160	2
Exon	18,603,581	18,603,641	61	0
Exon	18,600,112	18,600,200	89	2
Exon	18,595,392	18,595,440	49	0
Exon	18,588,020	18,588,155	136	1
Exon	18,586,660	18,586,751	92	0
Exon	18,586,312	18,586,558	247	1
Exon	18,572,792	18,572,898	107	0
Exon	18,571,137	18,571,287	151	1
Exon	18,566,911	18,567,071	161	0
Exon	18,564,312	18,564,496	185	2
Exon	18,562,724	18,562,793	70	0
Exon	18,559,871	18,559,965	95	2
Exon	18,550,309	18,550,474	166	0
Exon	18,549,076	18,549,169	94	1
Exon	18,548,733	18,548,821	89	0
Exon	18,547,713	18,547,901	189	0
Exon	18,546,878	18,547,037	160	1
Exon	18,540,097	18,540,167	71	0
Exon	18,539,801	18,539,889	89	2
Exon	18,535,128	18,535,206	79	0
Exon	18,534,744	18,535,005	262	1
Exon	18,533,539	18,533,746	208	2
Exon	18,531,345	18,531,348	4	0
UTR	18,529,703	18,531,344		

Catalytic activity: ATP + a protein = ADP + a phosphoprotein.

Enzyme reactions

Reaction: ATP + a protein = ADP + a phosphoprotein



Enzyme regulation: Activated by RHOA binding. Inhibited by Y-27632. Binding site 105 Active site 198 Nucleotide binding- 82 90 Zink finger -1228 1281.

Taxonomic lineage of the protein is as follows
Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Eutheria › Euarchontoglires › Primates › Haplorrhini › Catarrhini › Hominidae › Homo

Structural alignment of the protein

Protein namesi Recommended name:
Rho-associated protein kinase 1 (EC: 2.7.11.1)

Alternative name(s):
Renal carcinoma antigen NY-REN-35
Rho-associated, coiled-coil-containing protein kinase 1
Rho-associated, coiled-coil-containing protein kinase I
Short name: ROCK-I p160 ROCK-1
Short name: p160ROCK
Gene namesi Name: ROCK1
Organismi Homo sapiens (Human)
Taxonomic identifieri 9606 [NCBI]

Structural comparison of the protein

Chromosome 18PDB ID	Chain ID	Protein Name	Pfam ID	SCOP ID	UniProt ID	Z-Score
3o0z	C	Rho-associated protein kinase 1	PF02185		Q13464	4.6
2c08	A	Sh3-containing grb2-like protein 2	PF03114	a.238.1.1	O35179	2.84
2fxm	A	Myosin heavy chain, cardiac muscle beta isoform		h.1.26.1		2.73
2oqq	B	Transcription factor hy5	PF00170		O24646	2.65
2v66	B	Nuclear distribution protein nude-like 1	PF04880		Q9GZM8	2.6
2pih	A	Protein ymca	PF06133	a.281.1.1	O31779	2.58
3ssu	A	Vimentin	PF00038 PF04732		P08670	2.55
1s2x	A	Cag-z	PF09053	a.47.3.1	Q9JMX9	2.54
2v71	A	Nuclear distribution protein nude-like 1	PF04880		Q78PB6	2.53
1joc	A	Early endosomal autoantigen 1	PF01363	g.50.1.1 h.1.21.1	Q15075	2.53
3swk	A	Vimentin	PF00038		P08670	2.51
1m1j	A	Fibrinogen alpha subunit	PF00147 PF08702 PF12160	h.1.8.1	P14448	2.5
3ni0	A	Bone marrow stromal antigen 2				2.5
2f9d	P	Splicing factor 3b subunit 1	PF08920		O75533	2.47
2ykt	A	Brain-specific angiogenesis inhibitor 1-associated protein 2	PF08397		Q9UQB8	2.45
1r8i	A	Trac	PF07996	a.8.7.1	Q9L6G5	2.45

Taxonomic lineage

Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Eutheria › Euarchontoglires › Primates › Haplorrhini › Catarrhini › Hominidae › Homo

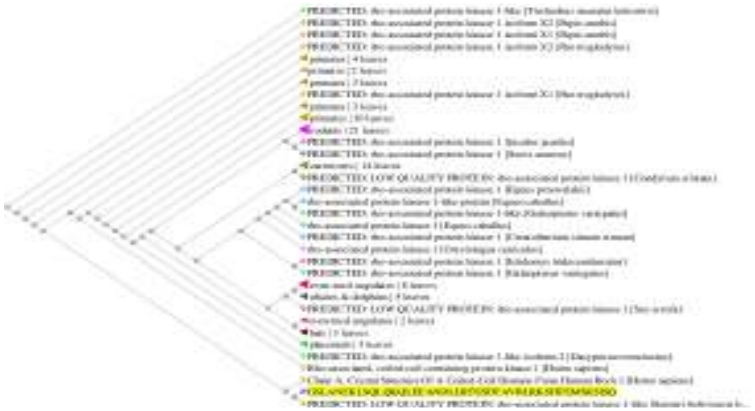
Secondary Structure prediction by DSSP

89% helical (2 helices; 150 residues

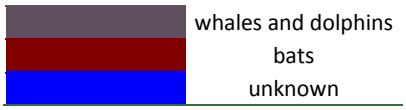
Fasta format of the amino acid sequence

>3O0Z:D|PDBID|CHAIN|SEQUENCE
GSLANEKLSQLQKQLEEANDLLRTESDTAVRLRKS
HTEMSKSISQLESLNRELQERNRILENSKSQTDKDY
YQLQAILEAERRDRGHDSEMIGDLQARITSLQEEV
KHLKHNLEKVEGERKEAQDMLNHSEKEKNNLEID
LNYKLKSLQQRLEQEVNEHKVTKARLTD

Phylogenetic Tree of the protein



Blast names color map
placentals
primates
rodents
insectivores
carnivores
odd-toed ungulates
rabbits and hares
even-toed ungulates

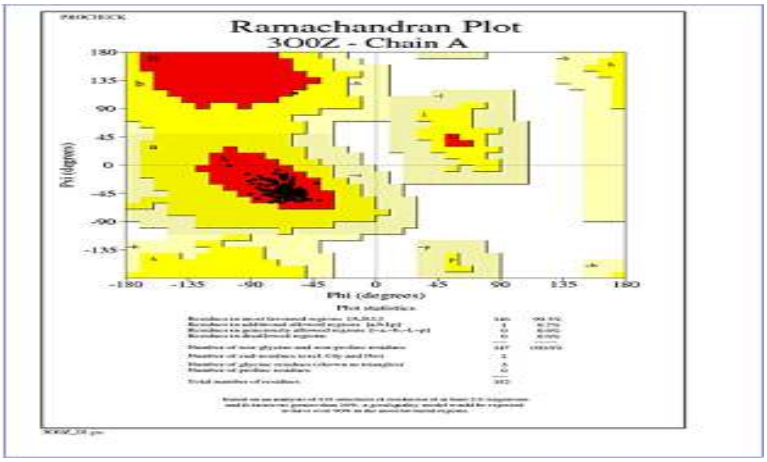


Tree Method: Fast Minimum Evolution
Max Seq Difference: 0.85
Distance: Grishin
Tree is based on COBALT multiple alignment. This gene encodes a protein serine/threonine kinase that is activated when bound to the GTP-bound form of Rho. The small GTPase Rho regulates formation of focal adhesions and stress fibers of fibroblasts, as well as adhesion and aggregation of platelets and lymphocytes by shuttling between the inactive GDP-bound form and the active GTP-bound form. Rho is also essential in cytokinesis and plays a role in transcriptional activation by serum response factor. This protein, a downstream effector of Rho, phosphorylates and activates LIM kinase, which in turn, phosphorylates cofilin, inhibiting its actin-depolymerizing activity. [provided by RefSeq, Jul 2008]
Function: EC: non-specific serine/threonine protein kinase; Transferases; Transferring phosphorous-containing groups;Protein-serine/threonine kinases (2.7.11.1)
Ramachandran Plot: Ramachandran Plot Analysis
The number of residues in favoured region are 98.9%

Evaluation of residues

- Residue [A 617 :ARG] (-42.79, -28.84) in Allowed region
- Residue [B 580 :SER] (-57.27, -69.54) in Allowed region
- Residue [B 688 :VAL] (-44.48, -29.66) in Allowed region
- Residue [C 537 :ASN] (-42.95, -62.42) in Allowed region
- Residue [C 581 :LEU] (-41.31, -35.70) in Allowed region
- Residue [C 595 :SER] (-35.69, -55.80) in Allowed region
- Residue [D 586 :GLN] (-55.62, -13.14) in Allowed region
- Number of residues in favoured region (~98.0% expected): 608 (98.9%)

Number of residues in allowed region (~2.0% expected): 7 (1.1%)
Number of residues in outlier region: 0 (0.0%)



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