



Structural Analysis and Molecular Mechanics of Pxr1 Gene which is Responsible For Zellweger Syndrome

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Abstract

Zellweger syndrome is an autosomal recessive disorder caused by mutations in genes that encode peroxins, proteins required for the normal assembly of peroxisomes. It causes a defect in the peroxisomes, which affects the body severely. It affects both males and females and is present at birth. The target gene coding protein in Zellweger syndrome had been identified. Blast P is used for the similarities identification of pxr1 protein and the Functional identification of pxr1 is viewed through AMIGO. Secondary structural analyses of pxr1 protein were carried through tools like, TARGET P, GLOBPROT, and DOMAIN LINKER PREDICTION. From the molecular mechanics study, the electrostatic properties have been identified.

INTRODUCTION

Zellweger syndrome, also called cerebrohepatorenal syndrome, is a rare congenital disorder, characterized by the reduction or absence of functional peroxisomes in the cells of an individual¹. It is one of a group of four related diseases called peroxisome biogenesis disorders (PBD), which are part of a larger group of diseases known as the leukodystrophies². These are inherited conditions that damage the white matter of the brain and also affect how the body metabolizes particular substances in the blood and organ tissues. They are caused by defects in any one of 12 genes, termed PEX genes that are required for the normal formation and function of peroxisomes (cell structures that break down toxic substances in the liver, kidneys, eyes, and brain, and synthesize fatty materials that are necessary for cell function). Peroxisomes are required for normal brain development and the function and formation of myelin, the whitish material that coats nerve fibers³.

Zellweger syndrome is an inherited peroxisomal metabolic disorder. Peroxisomes are found in almost all body cells and are responsible for many important cellular processes. Zellweger syndrome causes a defect in the peroxisomes, which affects the body severely (Fig – 1). Zellweger syndrome is estimated to occur in 1 of every 50,000 to 100,000 births. It affects both males and females and is present at birth⁴. Peroxisomes are usually abundant in a person's kidney and liver.

Peroxisomes are cell structures that break down toxic substances and synthesize lipids (fatty acids. Oils, and

waxes) that are necessary for cell function. Peroxisomes are required for normal brain development and function and the formation of myelin, the whitish substance that coats nerve fibers⁵. They are also required for normal eye, liver, kidney, and bone functions. Zellweger spectrum disorders result from dysfunctional lipid metabolism, including the over-accumulation of very long-chain fatty acids and phytanic acid, and defects of bile acids and plasmalogens--specialized lipids found in cell membranes and myelin sheaths of nerve fibers. Symptoms of these disorders include an enlarged liver; characteristic facial features such as a high forehead, underdeveloped eyebrow ridges, and wide-set eyes; and neurological abnormalities such as mental retardation and seizures⁶. Infants with Zellweger syndrome also lack muscle tone, sometimes to the point of being unable to move, and may not be able to suck or swallow. Some babies will be born with glaucoma, retinal degeneration, and impaired hearing. Jaundice and gastrointestinal bleeding also may occur.

AIM AND OBJECTIVES

To find out the mutational genes involved in Zellweger syndrome. To predict 3D Structure of the Protein. To visualize molecular mechanics of the protein.

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METHODOLOGY

Zellweger syndrome is the most severe of three PBD disorders that have overlapping features; the other disorders being neonatal adrenoleukodystrophy and Infantile Refsum Disease, the mildest disorder⁷. The National Center for Biotechnology Information (NCBI) provides a comprehensive website for biologists that includes biology-related databases, and tools for viewing and analyzing the data inherent in the databases. Basic Local Alignment Search Tool, or BLAST, is an algorithm for comparing primary biological sequence information, such as the amino-acid sequences of different proteins or the nucleotides of DNA sequences. . AmiGO is the official web-based set tools for searching and browsing the Gene Ontology database, which consists of a controlled vocabulary of terms covering biological concepts, and a

large number of genes or gene products whose attributes have been annotated using Gene Ontology terms. ClustalW starts by finding the score of the Multiple alignment between each pair of sequences, using a scoring function that is appropriate for proteins. Target to predict the subcellular location of eukaryotic proteins. GlobPlot is a web service that allows the user to plot the tendency within the query protein for order/globularity and disorder. Domain Linker Prediction-SVM is a domain linker predictor. It is composed of three loops-length dependent SVM predictors of domain linkers (SVM-All, SVM-Long and SVM-Short), and SVM-Joint, which combines the results of SVM-Short and SVM-Long into a single consolidated prediction. DIPOLE MOMENT SERVER used to predict Electrostatic properties of the target proteins.

Figure: 1



RESULTS AND DISCUSSION

1. NCBI-SEQUENCE RETREIVAL

PROTEIN

>gi|223590138|sp|A5DRH5.2|PXR1_PICGU RecName: Full=Protein PXR1; AltName: Full=PinX1-related protein 1

MGLAGTKVKQRFGLDPRNTSWSNDKSRFGHRYLESMGWAPGKGLGLVEHATTTTHVKVSVKDDTVGLGL

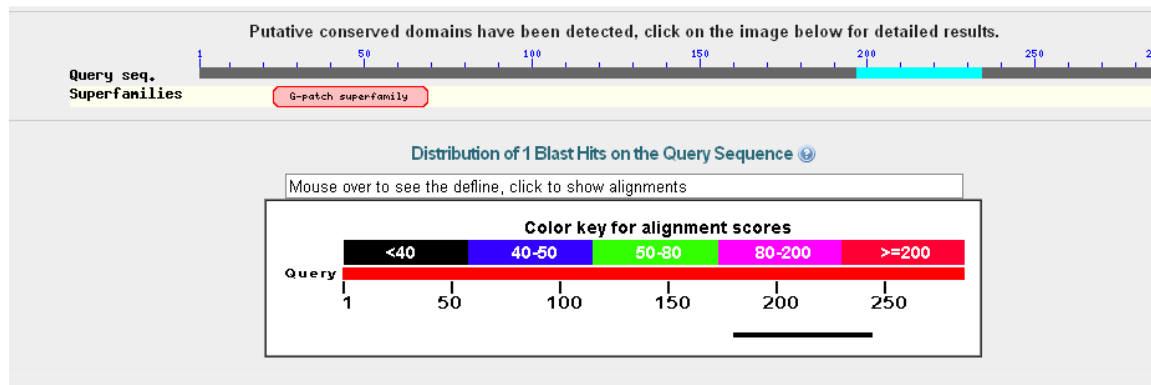
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AKRSGTDDLETSSGLDDFQRLGRLNGRGREVDLEQKRKDNIIINGKWMHFQKGEVLCSTWDRKSKS
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KKEKKEKKEKKEKKEKKEKKEKRDYGNRASPVPRKHDQISNVGRLSARAKYIKQKRASVMDAKAK
NUCLEOTIDE
>gj|359750250:9857-12145 Torulaspora delbrueckii CBS 1146 chromosome 7, complete genome
TTAAAAGAGACAAACGAGGGACAACAACAGAACTGACAGTGATGATCTCACACGTGCCGCAGAGCCCTCG
TAGGACGTTAGGCTTGCCTGAGTATGAATAGATGCGAAACCAGTCGAAGAAGGCTCGCTTTTGGAAATAC
TTGATGTTGAAGCGGGTGCCTGACTGATCGTAGTCATAGTACTTTGCAACCCACTAACAACCTTCAGATTG
GCCAGAAAGTTGTTGATTAGTCGTTGCAGAAGCATGAGTTGAACTTGGATTGAGGATAAAGTCTCACCA
TAGTTTATGGTCGAGGCCACAGAGCTTAGGGATTCTGTAGGAGCTATGTGGCTTCCGGGTATCGAAAGGG
TGGTAGTTCGATGGGATCTAACTTTTGTAAACGTAGCAGTAGTGCCTTCTGAGGAAGATGTTACCGAAAC
ACCTGTGTCAGTTGACGTCTCGGGTAATTGTGATACCTCACTGCTTTGAGCACAAAGCTTCACACTCTACC
TGACTTTGAATCCCTATAGATCCACTAGAGGCTGGAGATGGGGTCAACGTTACTGGGCTTCTTGGAACGA
AGGTAGCGGAATTTTGTGTGGAGTCCGTGCTATCAGACCTTGAGCAGGTTACGAAAGGTGCAGAATCAGA
TGATACCAAAGCGTAGAATTAGGTGGTACCAATGTGCAACTAGATAGTCCGGAGCAGCTACGGATAGAA
ACTACCACCGTAGAAGTAGTTCCATAACGGATGTATAGCTGGGTAGTACCGATGTAGAAGTACTTGCCA
CTAAAAATGTAGAACCAGATGCAATCGAAGTAGAAGGTAAGTGGTTCGAGCTAGATGCAGAACCAGA
TAGTGCTGAAGAAGCGGAGCTAGATGGTGTGAAGACGCAGAGCTAGATGGTGCAGATGATATCCATGAA
GCTGGTTGCTTTGTGGTGTAGCTGGCACTGAAGTAGTTGAGCTAGATGCAGAGCTAGATGGTGTGTAAG
ACGCAGAACTAGATGGTGGTGTGATGTCCATGAAGCTGGTTGCTTTGTGGTGTAGCTGGCACTGAAGT
GGTCGAGCTAGATGCAGAGCTAGATGGTGTGAAGACGCAGAGCTAGATGGTGCAGATGATATCCATGAA
GCTGGTTGCTTTGTGGTGTAGCTGGCACTGAAGTGGTCGAGCTAGATGCAGGGTTAGATGGTGCCGAAG
ACGTAGAACTAGATGGTGCAGCAATGTGCAACTAGATGATGTGGAGGATGCAGCGCTAGATCTAGAGTT
AGATGAAACCAAGACTTGGAGCTAGTTGGTTGTAATGTTTTGTAGTAGAACCAGGAACAGATGACGAT
GAAGAAGCGGAGCTATGCGCAGAGCTAATAGAAGCGGAGTTAGATGGCACTGACGATATCCAACCTGGCTG
GTTCCCTTGTAGTGCTAGCTGGCACTGAAGTAGTTGAGCTAGATGCTGAGCTAGAAGATGTCGAACTAGG
ACTGCTTGTGCTTATTGGGACTGATGTGGCAGAGCTAGAAGCTGACGGTACCGAAGAAGTAGATTTAGAT
GGTGCTGAAGTCGTCAAAATAGAAACAGAGCTAGCTGGCTCCTTTGTGGTACTAGCTGGCACTGAAGACG
TGGAGCTTGTGGAGCTGGTAGAGCTTGTGGAGCTGGTAGAGCTTGTGGAGCTGGTAGAGCACTTAGCATT
ATCCAGTACCATAGCGAAAGTCAGCATTAGAATTGCCATTGTTGTCTGCGTTACAACCAGTCATCAAAA
TCAAAAGCAGTTGCACCCCATTTCCAAGTTTCCAGTACTGAGCGGCATCACCTTGCAGATACTCGTATT
GAATTTGGAATGATGGCATAGCAACTTTACATTCATCGCCATTATACTTTTGACCATAAACTTGAATTTT
CGTCGTGAAATCTGTCGGGTTATCAATTATATAGGTATTCTCATTCTTACCCCAAAGTTGTTTAGTACCC
ATTGGACCATTGATGCCAATGATTTTTAAGGAATAGAGATACTTCATATCAATCTGTTGATCACCCCTTGA
CATTTATTGAAAGTTCATAAGTATTGTCACCGACCCAATCGACTGACAATAGATCCATGTAATATGGCAT
GGTGTGGTATTTTTTGCCTGACATTTGAAGTTCAAATTTGGACACATATTAGTAACTCCAGACACAGCT
GACGATGTGCGGCGAACTAACGCTGAATCACCATTATTAGAATAAAAATCAGTCTCGTAAGTATTATCGG
AGGCTGCTGAAGCAACCCCTAACAAACATAAGAGCAGATAGGAAAGCAT

```

The above results show the FASTA format sequence of PXR1.

2. BLAST P



Sequences producing significant alignments:						
Accession	Description	Max score	Total score	Query coverage	E value	Max ident
3KZ4_A	Chain A, Crystal Structure Of The Rotavirus Double Layered	33.5	33.5	22%	0.16	34%

The above result shows the similarity search of PXR1.

3. FUNCTIONAL IDENTIFICATION-AMIGO

rel ↓	Symbol, full name	Species
<input type="checkbox"/>	PXR1 Essential protein involved in rRNA and snoRNA maturation	10 associations gene from <i>Saccharomyces cerevisiae</i>
<input type="checkbox"/>	Pex5 ★ peroxisomal biogenesis factor 5	32 associations protein from <i>Mus musculus</i>
<input type="checkbox"/>	PEX5 Peroxisomal targeting signal 1 receptor	14 associations protein from <i>Bos taurus</i>
<input type="checkbox"/>	PEX5 ★ Peroxisomal targeting signal 1 receptor	15 associations protein from <i>Homo sapiens</i>
<input type="checkbox"/>	PEX5 Peroxisomal targeting signal 1 receptor	7 associations protein from <i>Cavia porcellus</i>
<input type="checkbox"/>	F1:PXR1 Guanylate cyclase	6 associations protein from <i>Canis lupus familiaris</i>

The above result shows the functional identification of PXR1.

4. PHYLOGENETIC ANALYSIS

CLUSTAL 2.1 multiple sequence alignment

```

sp|O70525|PEX5_CAVPO      MAMRELVEGECGGANPLMKLAGHFTQDKALRQEGLRPGWPPGAPASETV 50
sp|P50542|PEX5_HUMAN     MAMRELVEAECGGANPLMKLAGHFTQDKALRQEGLRPGWPPGAPASEAA 50
sp|O09012-2|PEX5_MOUSE  MRELVEGECGGANPLMKLATHFTQDKALRQEGLRPGWPPGASAAETV 50
gi|285812468|tpg|DAA08368.1|MGLAATRTRKQRFGLDP--RNTAWSNDTSRFGHQFLEKFGWKPGMGLGLSP 48
      *.:  : *.* :. :. :. :. *  ***  .:

sp|O70525|PEX5_CAVPO      SKPLGVASEDELVAEFLQDQNAPLVSRAPQTFKMDLLAEMQEIEQSNFR 100
sp|P50542|PEX5_HUMAN     SKPLGVASEDELVAEFLQDQNAPLVSRAPQTFKMDLLAEMQQIEQSNFR 100
sp|O09012-2|PEX5_MOUSE  SKPLGVGTEDELVSEFLQDQNA TLVSRAPQTFKMDLLAEMQEIEQSNFR 100
gi|285812468|tpg|DAA08368.1|  MN-----SNTSHIKVSIKDDNVGLGAKLKRKDKKDEFD----- 81
      :  .: : **.* *.: : * *.:

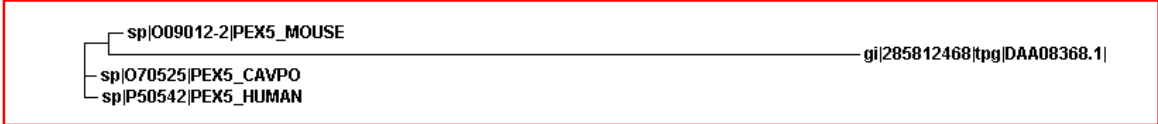
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sp|P50542|PEX5_HUMAN     QAPQRAPGVADLALSENWAQEFLAAGDAVDVTQDYNETDWSQEFISEVTD 150
sp|O09012-2|PEX5_MOUSE  QAPQRAPGVADLALSENWAQEFLAAGDAVDVAQDYNETDWSQEFIAEVD 150
gi|285812468|tpg|DAA08368.1|  -----NGECAGLDVFRILG 96
    
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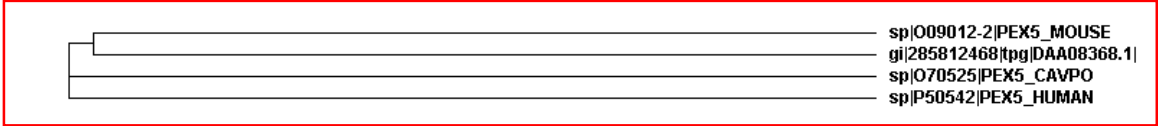
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sp|P50542|PEX5_HUMAN     PLSVSPARWAEELYEQSEKWLWLGEPEGTAT-DRWYDEYHPEEDLQHTAS 199
sp|O09012-2|PEX5_MOUSE   PLSVSPARWAEELYEQSEKWLWLDQEGSSTADRWYDEYHPEEDLQHTAS 200
gi|285812468|tpg|DAA08368.1|  RLNGKESKISEELDTRKQKIIDG-----KWGIHFVKGEVLAETWD 137
                                * . . . . .
                                * . . . . *
                                * . . . . *
                                * . . . . *
sp|O70525|PEX5_CAVPO      DFVAKVDDPKLANSEFLKFVRQIGEGQVSLVAGSGRAQAEQWAAEFIQ 250
sp|P50542|PEX5_HUMAN     DFVAKVDDPKLANSEFLKFVRQIGEGQVSLVAGSGRAQAEQWAAEFIQ 249
sp|O09012-2|PEX5_MOUSE   DFVSKVDDPKLANSE----- 215
gi|285812468|tpg|DAA08368.1|  PKTHKLRN----- 145
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      QQGTSDAWVDQFTRPVN-TSALDMEFERAKSAIESDVDFWDLQAELEEM 299
sp|P50542|PEX5_HUMAN     QQGTSDAWVDQFTRPVN-TSALDMEFERAKSAIESDVDFWDLQAELEEM 298
sp|O09012-2|PEX5_MOUSE   --GTSEAWVDQFTRPGNKIAALQVEFERAKSAIESDVDFWDLQAELEEM 263
gi|285812468|tpg|DAA08368.1|  -----YSNAK-----KRKREGDDS 159
                                . . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      AKRDAEAHPWLSYDDLTASADYDGYQFEENPLRDHPQPFEEGLLRLEE 349
sp|P50542|PEX5_HUMAN     AKRDAEAHPWLSYDDLTASADYDGYQFEENPLRDHPQPFEEGLLRLEE 348
sp|O09012-2|PEX5_MOUSE   AKRDAEAHPWLSYDDLTASADYDGYQFEENPLRDHPQPFEEGLLRLEE 313
gi|285812468|tpg|DAA08368.1|  EDEDDDDK----EDKDSDKKKHKKHKKHKKDKKKDKKDKKEHKKHKKEE 204
                                * . . . .
                                * . . . . *
                                * . . . . *
                                * . . . . *
sp|O70525|PEX5_CAVPO      GDLPNAVLLFEAAVQQDPKHMEAWQYLGTTQAENEQELLAISALRRCLEL 399
sp|P50542|PEX5_HUMAN     GDLPNAVLLFEAAVQQDPKHMEAWQYLGTTQAENEQELLAISALRRCLEL 398
sp|O09012-2|PEX5_MOUSE   GDLPNAVLLFEAAVQQDPKHMEAWQYLGTTQAENEQELLAISALRRCLEL 363
gi|285812468|tpg|DAA08368.1|  KRLK-----KEKRAEKTKETKTSKL 225
                                *
                                * . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      KPDNRTALMALAVSFTNESLQRQACETLRDWLRCTPAYAHLVTPAEEGAG 449
sp|P50542|PEX5_HUMAN     KPDNQTALMALAVSFTNESLQRQACETLRDWLRCTPAYAHLVTPAEEGAG 448
sp|O09012-2|PEX5_MOUSE   KPDNRTALMALAVSFTNESLQRQACETLRDWLRCTPAYAHLVTPAEEGAG 413
gi|285812468|tpg|DAA08368.1|  KSSESASNIPDAVNTR-----LSVRSKWIKQK----- 252
                                * . . . .
                                * . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      GAGLGSSKRILGSLSDSLFLEVKEFLAAVRLDPTSIDPDVQCGLGVLF 499
sp|P50542|PEX5_HUMAN     GAGLGPSKRILGSLSDSLFLEVKEFLAAVRLDPTSIDPDVQCGLGVLF 498
sp|O09012-2|PEX5_MOUSE   GA--GPSKRILGSLSDSLFLEVKEFLAAVRLDPTSIDPDVQCGLGVLF 461
gi|285812468|tpg|DAA08368.1|  -----RAALMDSKALNEIFMITND----- 271
                                . . . . .
                                * . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      NLSGEYDKAVDCFTAALSVRPNDYLLWNKLGATLANGNQSEEAVAAAYRRA 549
sp|P50542|PEX5_HUMAN     NLSGEYDKAVDCFTAALSVRPNDYLLWNKLGATLANGNQSEEAVAAAYRRA 548
sp|O09012-2|PEX5_MOUSE   NLSGEYDKAVDCFTAALSVRPNDYLLWNKLGATLANGNQSEEAVAAAYRRA 511
gi|285812468|tpg|DAA08368.1|  -----
                                * . . . .
                                * . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      LELQPGYIRSRYNLIGISCINLGAHREAVEHFLEALNMQRKSRGPRGEGGA 599
sp|P50542|PEX5_HUMAN     LELQPGYIRSRYNLIGISCINLGAHREAVEHFLEALNMQRKSRGPRGEGGA 598
sp|O09012-2|PEX5_MOUSE   LELQPGYIRSRYNLIGISCINLGAHREAVEHFLEALNMQRKSRGPRGEGGA 561
gi|285812468|tpg|DAA08368.1|  -----
                                * . . . .
                                * . . . .
                                * . . . .
                                * . . . .
sp|O70525|PEX5_CAVPO      MSENIWSTLRLALSMLGQSDAYRAADARDLSALLALFGLSQ 640
sp|P50542|PEX5_HUMAN     MSENIWSTLRLALSMLGQSDAYGAADARDLSTLLTMFGLPQ 639
sp|O09012-2|PEX5_MOUSE   MSENIWSTLRLALSMLGQSDAYGAADARDLSALLAMFGLPQ 602
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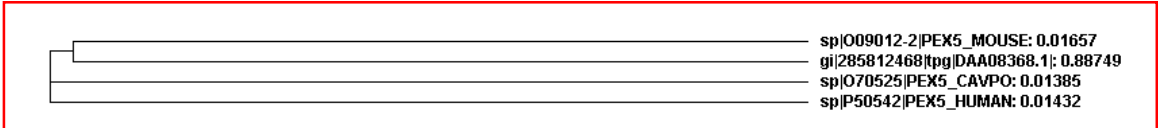
GUIDE TREE



CLADOGRAM TREE



DISTANCE TREE



The above result shows the phylogenetic analysis of PXR1.

5.STRUCTURAL ANALYSIS

A.TARGETP

targetp v1.1 prediction results

Number of query sequences: 1

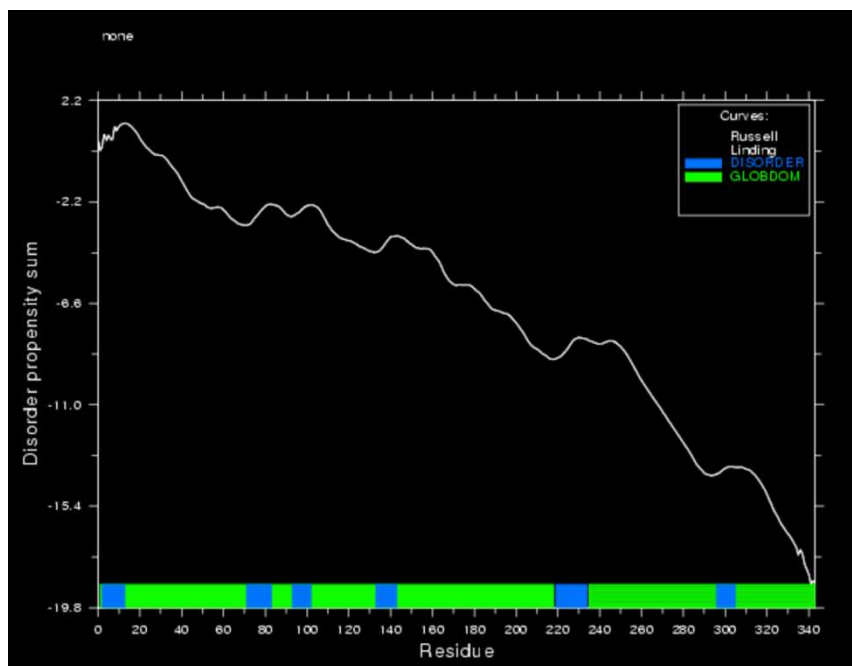
Cleavage site predictions not included.

Using NON-PLANT networks.

Name	Len	mTP	SP	other	Loc	RC
gi_223590138_sp_A5DR	286	0.440	0.038	0.614	_	5
cutoff		0.000	0.000	0.000		

The above result shows the transmembrane reigns in the PXR1.

B.GLOBPLOT



Disordered by Russell/Linding definition

```
>none_Disorder 2-13, 71-83, 93-102, 133-143, 219-234, 296-305
gISPADRHPR PICgrecnam efillprtein praltnamef llpinrelat edprteinmg lagtkvkqrf GLDPRNTSWS
NDKsrfgghry leSMGWAPGK GLglvehatt thvkvsvkdd tvglgaklak rsgTDDLETD SSGlddfqri lgrlngrgre
vdealeqkrk dniingkwgm hfikgevlcs twdrkskshM lktaledeSe vnfksskRR QSGSEPSRDS TSHAKRMrgd
eskkstrdqs kqerkekKik tekkekkekK kkekkekKek kerdyGNRAS PVEPRkhdqi snvgrlsara
kyikqkrasv mDakalneif misk
```

Potential globular domains (GlobDoms) by Russell/Linding definition

```
>none_GlobDoms 1-218, 235-344
GISPADRHPR PICGRECNAM ELLPRTEIN PRALTNAMef LLPINRELAT EDPRTINMG LAGTKVKQRF GLDPRNTSWS
NDKSRFGHRY LESMGWAPGK GLGLVEHATT THVKVSVKDD TVGLGAKLAK RSGTDDLETD SSGLDLDFQRI LGRINGRGRE
VDEALBQKRK DNIINGKWGM HFIKGEVLCs TWDRKSKSHM LKTALEDESE VNFKSSKRRr qsgsepsrds tshakRMrgd
ESKKSTRDQS KQERKEKKIK TEKKEKKEKK EKKEKKEKKE KKEKKEKKEK KERDYGNRAS PVEPRKHDQI SNVGRLSARA
KYIKQKRASV MDAKALNEIF MISK
```

JOB-ID: none_121427BWYRtgoLCBQAADgiisEAAAAL
Parameters: propensities=Russell/Linding smooth=10 dy/dx_smooth=10
Disorder frames: peak-frame=5 join-frame=4
Globularity frames: peak-frame=74 join-frame=15
Name: None
Description: None
Plot title/ID: None
Sequence length: 344
Download Results [smoothed raw dydx](#)

The above result shows the disorders regions of PXR1 protein.

C.DOMAIN LINKER PREDICTION

Candidate Region:

SVM-All

Rank	Peak Value	Peak Position	Region	Sequence
1	2.009	165	148 - 247	EDESEVNFKSSKRRRQSGSEPSRDSTSHAKRMRGDE SKKSTRDQSKQERKEKKIKTEKKEKKEKKEKKEKKEKKE KKEKKEKKEKKEKDYGNRASPVEPR
2	0.305	75	73 - 79	RSGTDDL

SVM-Long

Rank	Peak Value	Peak Position	Region	Sequence
1	1.406	245	205 - 247	KKEKKEKKEKKEKKEKKEKKEKKEKKEKKEKDYGNR ASPVEPR
2	1.192	167	156 - 190	KSSKRRRQSGSEPSRDSTSHAKRMRGDESKKSTRD

SVM-Short

Rank	Peak Value	Peak Position	Region	Sequence
1	1.494	191	178 - 200	RMRGDESKKSTRDQSKQERKEK
2	1.148	110	107 - 112	LEQKRK

- Campodarve I, Zellweger C, Irfan A, Drexler B, Mueller C. Patients with Acute Coronary Syndrome and Normal High-sensitivity Troponin. Department of Internal Medicine, Division of Cardiology, University Hospital, Basel, Switzerland; Paris Descartes University, Cardiology Department, Cochin Hospital, APHP, Paris, France.
- Ezgu E, Eminoglu T, Okur I, Gunduz M, Tumer L, Hasanoglu A, Dalgic B. An infantile case of Zellweger syndrome presented with Kabuki-like phenotype. Gazi University Faculty of Medicine, Department of Pediatric Metabolism, Division of Genetics and Molecular Diagnosis, Ankara, Turkey. fezgu@gazi.edu.tr
 - Thoms S, Grønberg S, Rabenau J, Ohlenbusch A, Rosewich H, Gärtner J. Characterization of two common 5' polymorphisms in PEX1 and correlation to survival in PEX1 peroxisome biogenesis disorder patients. Department of Pediatrics and Pediatric Neurology, University Medical Center, University of Göttingen, Robert Koch Str, 40, 37099 Göttingen, Germany. sven.thoms@med.uni-goettingen.de
 - Cho SY, Chang YP, Park JY, Park HD, Sohn YB, Park SW, Kim SH, Ji S, Kim SJ, Choi EW, Kim CH, Ko AR, Paik KH, Jin DK. Two novel PEX1 mutations in a patient with Zellweger syndrome: the first Korean case confirmed by biochemical, and molecular evidence. Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul, Korea.
 - Nakayama M, Sato H, Okuda T, Fujisawa N, Kono N, Arai H, Suzuki E, Umeda M, Ishikawa HO, Matsuno K. *Drosophila* carrying pex3 or pex16 mutations are models of Zellweger syndrome that reflect its symptoms associated with the absence of peroxisomes. Genome and Drug Research Center, Tokyo University of Science, Noda, Chiba, Japan
 - Mast FD, Li J, Virk MK, Hughes SC, Simmonds AJ, Rachubinski RA. A *Drosophila* model for the Zellweger spectrum of peroxisome biogenesis disorders. Department of Cell Biology, University of Alberta, Edmonton, AB T6G 2H7, Canada.
 - Kulkarni KS, Baranano KW, Lin DD, Raymond GV. Contrast enhancement of brainstem tracts in Zellweger spectrum disorder: evidence of inflammatory demyelination? School of Medicine, Johns Hopkins University Baltimore, Maryland 21287, USA. kopal@jhmi.edu
 - Ali BR, Hertecant JL, Al-Jasmi FA, Hamdan MA, Khuri SF, Akawi NA, Al-Gazali LI. New and known mutations associated with inborn errors of metabolism in a heterogeneous Middle Eastern population. Department of Pathology, Faculty of Medicine and Health Sciences, United Arab Emirates University, PO Box 17666, Al-Ain, United Arab Emirates. bassam.ali@uaeu.ac.ae
 - Brul S, W. A.; Westerveld, A.; Strijland, A.; Wanders, R.; Schram, A.; Heymans, H.; Schutgens, R.; Van Den Bosch, H. et al. (June 1988). "Genetic heterogeneity in the cerebrohepatorenal (Zellweger) syndrome and other inherited disorders with a generalized impairment of peroxisomal functions. A study using complementation analysis" (Free full text). *Journal of Clinical Investigation* 81 (6): 1710–1715. doi:10.1172/JCI113510. PMC 442615. PMID 2454948.