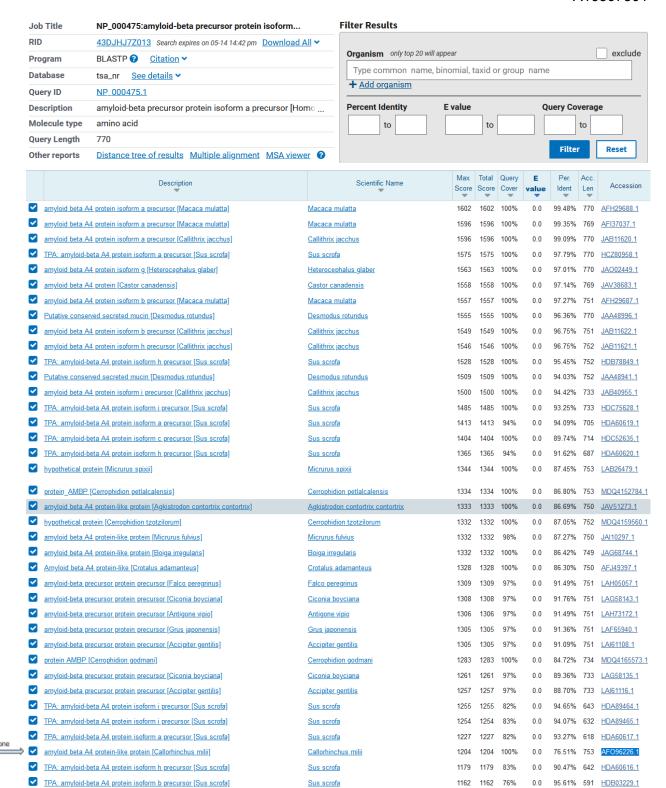
# Q1. Project Focus: Human APP

I will be looking into the amyloid beta precursor protein in humans because it has been associated with the buildup of beta-amyloid plaques seen in Alzheimers. The accession number for the A isoform is NP 000475.1.

According to Wikipedia, "**Amyloid-beta precursor protein** (**APP**) is an integral membrane protein expressed in many tissues and concentrated in the synapses of neurons. It functions as a cell surface receptor<sup>[5]</sup> and has been implicated as a regulator of synapse formation, <sup>[6]</sup> neural plasticity, <sup>[7]</sup> antimicrobial activity, <sup>[8]</sup> and iron export".

# Q2. Blastp of Human APP in tsa\_nr database



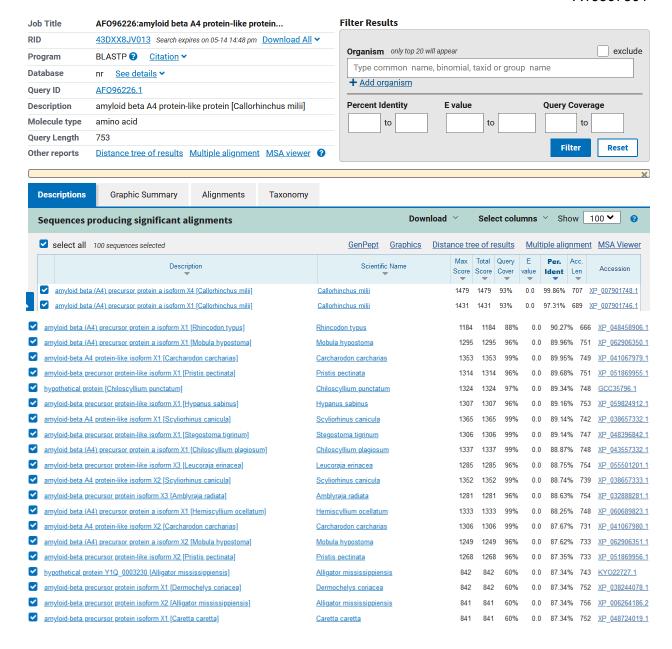
## Q3. Novel Gene Info

>AFO96226.1 amyloid beta A4 protein-like protein [Callorhinchus milii]
MFLQPAARLLLLSAIGTVTVSPSALTALEVPTDGGTGLLAAEPQIAMFCDKLNMHMNVQTGKWISDPSGT
NSCFGTKEGILQYCQEVYPDLQITNVVEANQPVTIQNWCKKGRKQCKGHPHIVIPYRCLVGEFVSDALLV
PDKCKFLHREKMDTCENHLYWHTVAKEACGDKTMNLKDYGMLLPCGIDQFRGVEFVCCPISEENEKVDSV
DVDEEDSYIWWGGADAEYSDGGDKVIEEEPMDEEEEVDIEDDDDEEEDEDDDDQYEDPTEHTTSSTTT
TTEAIEEVVREVCSEQAETGPCRAMIPRWYFDIGEGKCAQFIYGGCGGNRNNFDSEEYCLSVCSSVIPAT
AASTPDAIDQYLETPGDENEHAYFQKAKERQEARHRERMSQIMREWEEAERQARNLHKADKKAVIQRFQE
MVESLEQEAASERQQLVETHMARVEAMLNDRRRIALENYLAALQADPPRPRHVLNALKKYIRAEQKDRQH
TLKHFEHVRMVDPKKAAQIKSQVMTHLRVIDERMNQSLSLLYKVPAVAEEIQDEVDELLQKEQSYIDDMV
ANSVSDTRVSYGNDALVPSLSETKTTIELLPDQGEFTLDDLQPLHPFVVDSIPVNTENEVEPVDARPAAD
RGLTTRPGSGLTGIKTQEIAEVKMETKFRQDSGYEVHHQKLVFFPEDVGSNKGAIIGLMVGGVVIATVIV
ITLVMLKKKQYTSIHHGVIEVDAAVTPEERHLSKMQQNGYENPTYKFFEQMQN

This is the FASTA sequence for the amyloid beta A4 protein-like protein from Callorhinchus milii, the Australian Ghost Shark

## **Q4: Proving Novelty**

The output below shows that the this protein is indeed novel as the top hit does not match 100%.



# **Q5. Multiple Sequence Alignment**

Below is the MSA for the amyloid beta A4 protein-like protein sequences of 7 different species

CLUSTAL multiple sequence alignment by MUSCLE (3.8) Link: muscle-I20240529-195849-0477-60507466-plm

Human

MLPGLA--LLLL------AAWTARALEVPTDGNAGLL-AEPQIAMFCGRLNMHMNVQN

#### EasternCoralSnake

MLPHLA--LLLL-----GASWTAGALEVPTDGNAGLL-AEPQVAMFCGKSNMHMNVQN Copperhead

MLPHLA--FLLL------VASWTAGALEVPTDGNAGLL-AEPQVAMFCDKLNMHMNVQN BrownTreeSnake

MLPHLA--FLLL-----GASWTAGALEVPTDGNAGLL-AEPQVAMFCGKSNMHMNVQN AustralianGhostshark

MFLQPAARLLLLSAIGTVTVSPSALTALEVPTDGGTGLLAAEPQIAMFCDKLNMHMNVQT GreatWhiteShark

MIPHLPGRLRML-LVAAVIVLPSLCQALEVPTDGGTGLLAAEPQIAMFCGKLNMHMNVQS SmallSpottedCatshark

MIPHLPCRLRML--LAAAIVLSSLCRALEVPTDGGTGMLAAEPQIAMFCGKLNMHMNVQS
\*: . : \*\* \*\*\*\*\*\*\*.:\*:\* \*\*\*\*\*\*.. \*\*\*\*\*\*\*..

#### Human

GKWDSDPSGTKTCIDTKEGILQYCQEVYPELQITNVVEANQPVTIQNWCKRGRKQCKTHP EasternCoralSnake

 ${\tt GKWESDPSGTKSCITTKEGILQYCQQVYPELQITNVVEANQPVTIQNWCKQGRKQCRSHP} \\ {\tt Copperhead}$ 

GKWESDPSGTKSCIATKEGILQYCQQVYPELQITNVVEANQPVTIENWCKQGRKQCRSHP BrownTreeSnake

GKWESDPSGTKSCIATKEGILQYCQQVYPELQITNVVEANQPVTIQNWCKQGRKQCRSHP AustralianGhostshark

GKWISDPSGTNSCFGTKEGILQYCQEVYPDLQITNVVEANQPVTIQNWCKKGRKQCKGHP GreatWhiteShark

GKWVSDPSGTKSCFGTKEGILQYCQEVYPDLQITNVVEANQPVTIQNWCKKGRKQCKGHP SmallSpottedCatshark

## Human

HFVIPYRCLVGEFVSDALLVPDKCKFLHQERMDVCETHLHWHTVAKETCSEKSTNLHDYG EasternCoralSnake

YIVVPYRCLVGEFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKGMNLHDYG Copperhead

YIVVPYRCLVGEFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKEFCSEKGMNLHDYG BrownTreeSnake

YIVVPYRCLVGEFVSDALLVPDKCKFLHQERMDICETHLHWHTVAKESCSEKGMNLHDYG AustralianGhostshark

HIVIPYRCLVGEFVSDALLVPDKCKFLHREKMDTCENHLYWHTVAKEACGDKTMNLKDYG GreatWhiteShark

HIVVPYRCLVGEFVSDALLVPDKCKFLHREKVDTCESHLYWHTVAKETCGDKIMNLHDYG SmallSpottedCatshark

#### Human

MLLPCGIDKFRGVEFVCCPLAEESDNVDSADAEEDDSDVWWGGADTDYADGSEDKVVEVA EasternCoralSnake

MLLPCGIDKFRGVEFVCCLVVDESDNVDSAEAEEDDSDVWWGGADADYADGSYDKVTEEQ Copperhead

MLLPCGIDKFRGVEFVCCLVADESDNTDSTEAEEDDSDVWWGGADADYADGSYDKVTEEQ BrownTreeSnake

 ${\tt MLLPCGIDKFCGVEFVCCLVADESDNTDSAEAEEDDSDVWWGGADADYADGSYDKVTEEQ} \\ Australian Ghostshark$ 

MLLPCGIDQFRGVEFVCCPISEENEKVDSVDVDEEDSYIWWGGADAEYSDGG-DKVIEEE GreatWhiteShark

MLLPCGIDEFRGVEFVCCPIPEENDKIDDSDMDEEDSDVWWGGDDADYADGS-DKVIEEQ SmallSpottedCatshark

MLLPCGIDEFRGVEFVCCPIPEENDKIDS-DMDE-DSDVWWGGDDADYADGS-DKIIEEQ
\*\*\*\*\*\*\*\* \* \*\*\*\*\*\* : :\*.:: \*. : :\* \*\* :\*\*\*\* \*::\*:\*\*. \*\*: \*

#### Human

EEE-EVAEVEEEEADDDEDDEDGDEVEEEAEEPYEEATERTTSIATTTTTTESVEEVVR EasternCoralSnake

LAEGDTTDVEDENTDDDDDDE--DGXEVTEDQYQEAIERTTSIA-TTTTTTESVEEVVR Copperhead

LAEGDTTDIEDENTDDDDEDDD--EAEEVTEDQYQEATERTTSIA-TTTTTTESVEEVVR BrownTreeSnake

 ${\tt LAEGDTTDVEDENTDDDDXDXD--EAEEVTEDQYQEATERTTSIA-TTTTTTESVEEVVR} \\ Australian Ghostshark$ 

PMD-----EEEEVDIEDDDDEEEDEDDDDQYEDPTEHTTS---STTTTTEAIEEVVR GreatWhiteShark

PME-----EESDIDDEDDDDL---DGEEDEDQYEDPTEHTTS---STTTTTEAIEEVVR SmallSpottedCatshark

PME-----EESDIDDDLDGED------DEDQYEDPTEHTTS---STTTTTEAIEEVVR
: \*:: \*:: \*:: \*:: \*:\*\*\*\*\*

#### Human

EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSAMSQS EasternCoralSnake

EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSV----Copperhead

EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSV----BrownTreeSnake

EVCSEQAETGPCRAMISRWYFDVTEGKCAPFFYGGCGGNRNNFDTEEYCMAVCGSV---AustralianGhostshark

EVCSEQAETGPCRAMIPRWYFDIGEGKCAQFIYGGCGGNRNNFDSEEYCLSVCSSV----GreatWhiteShark

 $\label{thm:constraint} \begin{minipage}{0.5\textwidth} EVCSEQAETGPCQAMIPRWYFDISEGKCAQFIYGGCGGNRNNFASEEYCLAVCNSV----SmallSpottedCatshark \end{minipage}$ 

# Human LLKTTQEPLARDPVKLPTTAASTPDAVDKYLETPGDENEHAHFQKAKERLEAKHRERMSQ EasternCoralSnake ------IPTTAASTPDAVDKYLETPGDENEHSHFQKAKERLEAKHRERMSQ Copperhead -----IPTTAASTPDAVDRYLETPGDENEHSHFQKAKERLEAKHRERMSQ BrownTreeSnake -----IPTTAASTPDAVDKYLETPGDENEHSHFQKAKERLEAKHRERMSQ AustralianGhostshark -----IPATAASTPDAIDQYLETPGDENEHAYFQKAKERQEARHRERMSQ GreatWhiteShark -----IPTTAASTPDAVDKYLETPGDENEHAYFQKAKERLEAKHRERMSK SmallSpottedCatshark ------IPTTAASTPDAVDKYLETPGDENEHAYFQKAKERLEAKHRERMSK SmallSpottedCatshark -------LPTTAASTPDAVDKYLETPGDENEHAYFQKAKERLEAKHRERMSK :\*:\*\*\*\*\*\*\*\*\*

#### Human

VMREWEEAERQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR EasternCoralSnake

VMREWEEAEHQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR Copperhead

VMREWEEAEHQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR BrownTreeSnake

VMREWEEAEHQAKNLPKADKKAVIQHFQEKVESLEQEAANERQQLVETHMARVEAMLNDR AustralianGhostshark

IMREWEEAERQARNLHKADKKAVIQRFQEMVESLEQEAASERQQLVETHMARVEAMLNDR GreatWhiteShark

#### Human

RRLALENYITALQAVPPRPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS EasternCoralSnake

RRVALENYITALQAIPPKPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS Copperhead

RRVALENYITALQAVPPKPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS BrownTreeSnake

RRVALENYITALQAVPPKPRHVFNMLKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIRS AustralianGhostshark

RRIALENYLAALQADPPRPRHVLNALKKYIRAEQKDRQHTLKHFEHVRMVDPKKAAQIKS GreatWhiteShark

 $\label{lem:lal_qadppr} RRIALENYLAALQADPPRPRHVLNALKKYIRAEQKDRQHTLKHFEHVRMVDPKKAAQIKS \\ SmallSpottedCatshark$ 

RRIALENYLAALQADPPRPRHVLNALKKYVRAEQKDRQHTLKHFEHVRMVDPKKAAQIKS

#### Human

QVMTHLRVIYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISY EasternCoralSnake

QVMTHLRVTYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISY Copperhead

QVMTHLRVTYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISY BrownTreeSnake

QVMTHLRVTYERMNQSLSLLYNVPAVAEEIQDEVDELLQKEQNYSDDVLANMISEPRISY AustralianGhostshark

QVMTHLRVIDERMNQSLSLLYKVPAVAEEIQDEVDELLQKEQSYIDDMVANSVSDTRVSY GreatWhiteShark

QVMTHLRVIDERMNQSLSLLYKVPSVAEEIQDEVDELLQKEQSYIDDMVANSVSDTRISY SmallSpottedCatshark

#### Human

GNDALMPSLTETKTTVELLPVNGEFSLDDLQPWHSFGADSVPANTENEVEPVDARPAADR EasternCoralSnake

GNDALMPSLTETKTTVERLPVDGEFSLDDLQPWHPFAVDSVPANTENEVEPVDARPAADR Copperhead

GNDALMPSLTETKKTVEHLPVDGEFSLDDLQPWHPFAVDSVPANTENEVEPVDARPAADR BrownTreeSnake

GNDALMPSLTETK-TVEHLPVDGEFSLDDLQPWHPFAVDSVPANTENEVEPVDARPAADR AustralianGhostshark

GNDALVPSLSETKTTIELLPDQGEFTLDDLQPLHPFVVDSIPVNTENEVEPVDARPAADR GreatWhiteShark

GNDALVPSLSETKTTIELLPDDGEFNLDDLQPLHPFVIDSIPANTENEVEPVDARPAPDR SmallSpottedCatshark

#### Human

GLTTRPGSGLTNIKTEEISEVKMDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVG EasternCoralSnake

GLTTRPGSGLTNVKTEETSELKMDAEYRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVG Copperhead

GLTTRPGSGLTNVKTEETSELKMDAEYRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVG BrownTreeSnake

GLTTRPGSGLTNVKTEETSELKMDAEYRHDSGFEVHHQKLVFFAEDVGSNKGAIIGLMVG AustralianGhostshark

GLTTRPGSGLTGIKTQEIAEVKMETKFRQDSGYEVHHQKLVFFPEDVGSNKGAIIGLMVG GreatWhiteShark

GLTTRPGSGLTGIKTEGIAEVKMETEFRQDSGYEVHHQKLVFFPEDVGSNKGAIIGLMVG

## ${\tt SmallSpottedCatshark}$

#### Human

 ${\tt GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM} \\ {\tt EasternCoralSnake}$ 

GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM Copperhead

 ${\tt GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM} \\ {\tt BrownTreeSnake}$ 

 ${\tt GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM} \\ {\tt AustralianGhostshark}$ 

 ${\tt GVVIATVIVITLVMLKKKQYTSIHHGVIEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM} \\ {\tt GreatWhiteShark}$ 

GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM SmallSpottedCatshark

GVVIATVIVITLVMLKKKQYTSIHHGVVEVDAAVTPEERHLSKMQQNGYENPTYKFFEQM

Human QN
EasternCoralSnake QN
Copperhead QN
BrownTreeSnake QN
AustralianGhostshark QN
GreatWhiteShark QN
SmallSpottedCatshark QN
\*\*

# **Q6.** Phylogenetic Tree

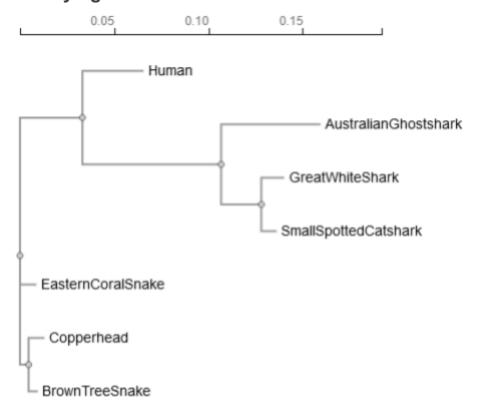


Fig.1 Phylogenetic tree for the MSA in Q5

# Q7. Heatmap

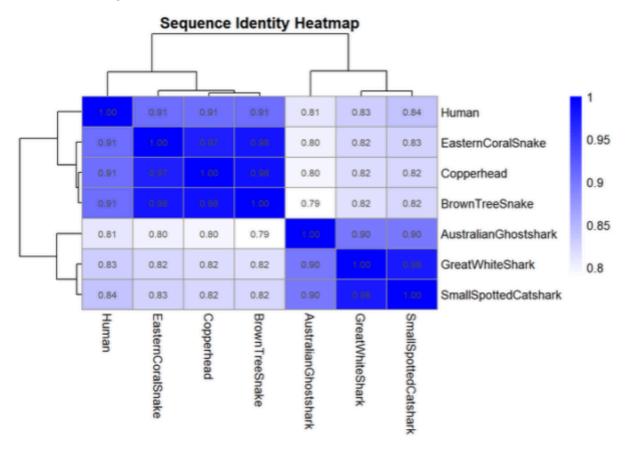


Fig 2. Sequence Identity Heatmap generated from the MSA in Q5

The heatmap shows 2 clusters: humans with snakes and sharks with each other

# **Q8. Blast PDB search of Consensus Sequence (EasternCoralSnake)**

Description	Scientific Name			Query	E value	Per. Ident	Acc. Len	
Chain A, Amyloid-beta precursor protein [Homo sapiens]	Homo sapiens	911	911	61%	0.0	92.45%	770	<u>80TF_A</u>
Chain A. Amyloid beta A4 protein [Homo sapiens]	Homo sapiens	683	683	45%	0.0	95.60%	342	5BUO_A
Chain B, Kunitz Protease Inhibitory Domain of Protease Nexin II [Homo sapiens]	Homo sapiens	134	134	7%	2e-37	98.25%	57	1ZJD_B

## Chain A, Amyloid-beta precursor protein (Homo sapiens)

Ab typeII filament from Guam ALS/PDC

PDB: 80TF

Source: Homo sapiens

Method: Electron Microscopy

Resolution: 3.3 Å E-value = 0.0 Seq Identity = 92.45%

## Chain A, Amyloid-beta A4 protein (Homo sapiens)

A receptor molecule

PDB: 5BUO

Source: Homo sapiens Method: X-ray Diffraction

Resolution: 2.31 Å E-value = 0.0

Seq Identity = 95.60%

## Chain B, Kunitz Protease Inhibitory Domain of Protease Nexin II (Homo sapiens)

Crystal Structure of the Catalytic Domain of Coagulation Factor XI in Complex with Kunitz Protease Inhibitor Domain of Protease Nexin II

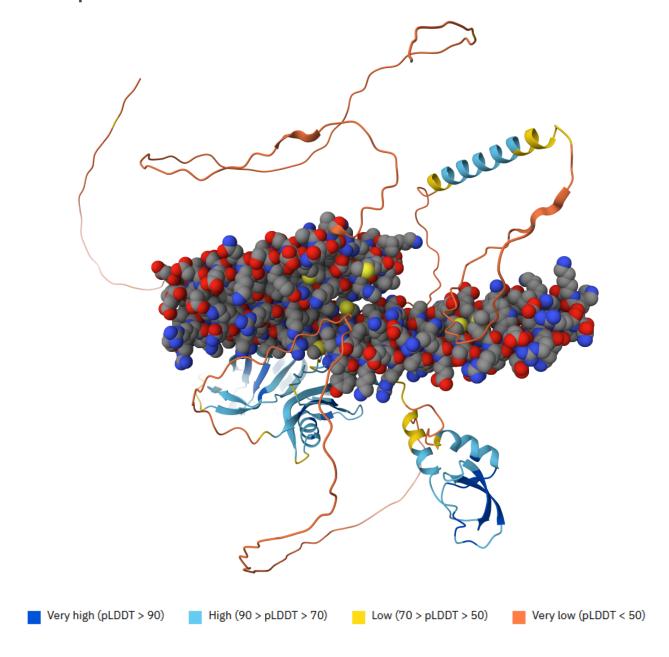
PDB: 1ZJD

Source: Homo sapiens Method: X-ray Diffraction

Resolution: 2.6 Å E-value = 2e-37

Seq Identity = 98.25%

# Q9. AlphaFold of Novel Protein



## Q10. ChEMBL Search for Novel Protein

#	E-Value	Positives %	Identities %	Score (bits)	Score	Length	ChEMBL ID	Name
1.	0	86.5	77.6	1226.08	3171	770	CHEMBL2487	Amyloid-beta protein
2.	0	87	77.8	1224.54	3167	770	CHEMBL3638365	Amyloid-beta protein
3.	0	86.9	77.8	1223.38	3164	770	CHEMBL4523942	Amyloid-beta protein
4.	6.2e-12	63.6	37.7	66.6254	161	304	CHEMBL3713062	Tissue fac pathway inhibitor
5.	3.6e-11	61.4	41.4	64.3142	155	306	CHEMBL4523142	Tissue fac pathway inhibitor

Target associated assays and ligand efficiency data are non listed as of 6/3/2024. The only information listed is that this protein is mostly found in eukaryotic cells in mammalia like primates and rodents. Most of the targets are unclassified, but there are many classified as enzymes and epigenetic regulators.

## ChEMBL Job ID:

BIOLOGICAL\_SEQUENCE\_SEARCH-pqZ2iRXxWDD58C1DxSEAaLyAa-Pv9pRprQDJrBscVQ w=