Master Biomedizin 2018

1) UCSC & UniProt
2) Homology
3) MSA
4) Phylogeny

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a. All of the sequences in "*file1.fasta*" (https://cbdm.uni-mainz.de/mb18/) are homologs. How many groups of orthologs would you say there are in this file? Use Trex (http://www.trex.uqam.ca/).
Two groups of orthologs: Protein A & protein B.

b. What could you say about the history of this protein family?
E.coli has only one protein, and then it duplicated to form A and B. It is possible that X.laevis_B duplicated later to form B and C.

c. Would you say there is any wrongly annotated sequence?
X.tropicalis_B is wrongly annotated. It should be X.tropicalis_A, because they are in the same branch. The actual X.tropicalis_B either is not in the dataset or was lost during evolution.

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Phylogeny

*Images from: Trex

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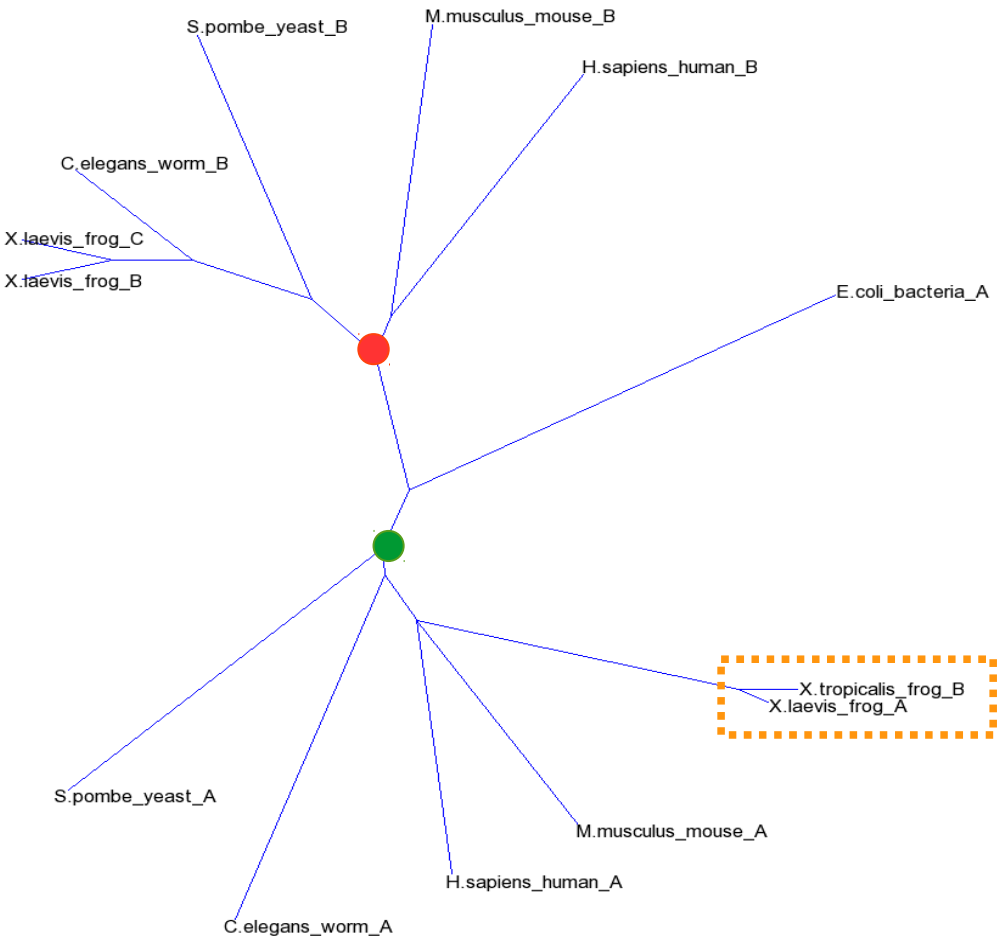

a. Two groups of orthologs:

- Proteins “A”
- Proteins “B”

b. E.coli has only one protein, and then it duplicated to form A and B. It is possible that X.laevis_B duplicated later to form B and C.

c. X.tropicalis_B is wrongly annotated. It should be X.tropicalis_A, because they are in the same branch. The actual X.tropicalis_B either is not in the dataset or was lost during evolution.

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a. Using "*file2.fasta*" (https://cbdm.uni-mainz.de/mb18/) and Trex (http://www.trex.uqam.ca/), can you approximate to which taxonomic division belongs "proteinX"? Primates.

b. From which organism could it be? After guessing, check it.
Homo sapiens (human) or *Pan troglodytes* (chimpanzee); they are 100% identical.

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Phylogeny

*Images from: Trex, UniProt

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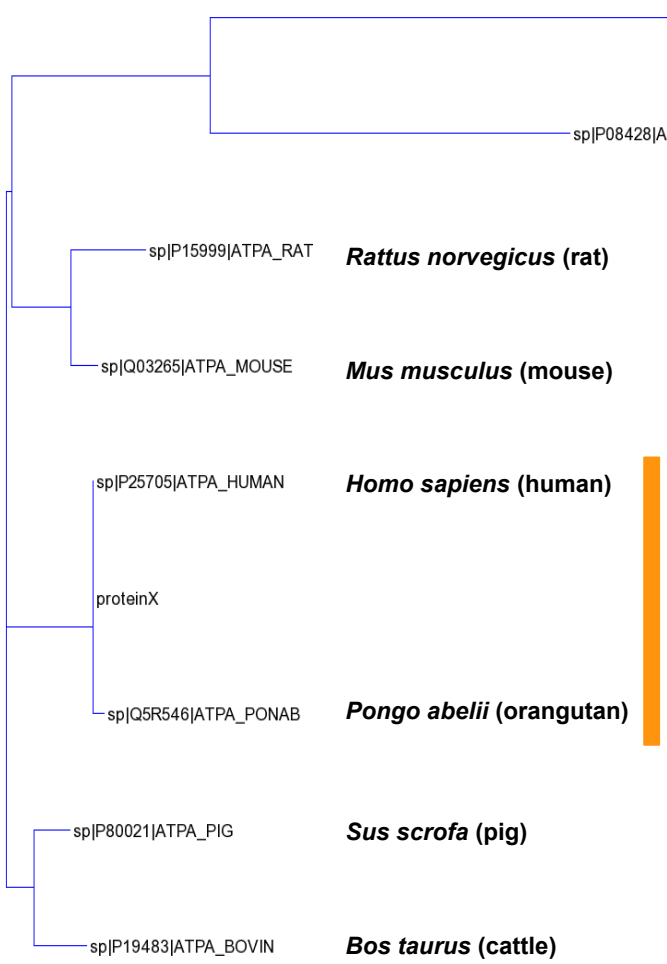
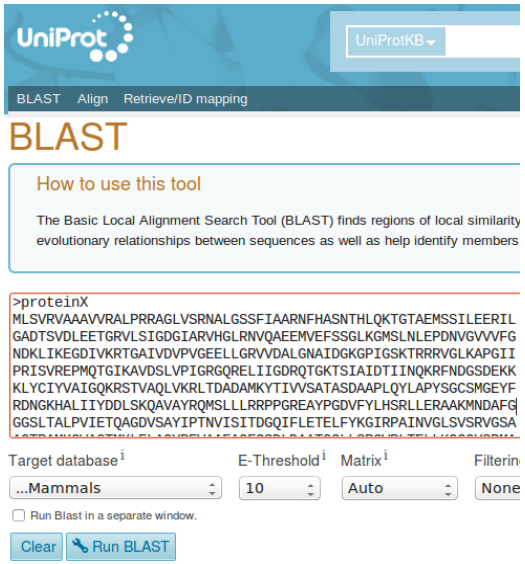


a. Primates



Entry	Protein names	Match hit (100 200 300 400 500)	Identity
P25705	ATP synthase subunit alpha, mitochondrial (Homo sapiens)		100.0%
A5A6H5	ATP synthase subunit alpha, mitochondrial (Pan troglodytes)		100.0%
V9HW26	ATP synthase subunit alpha (Homo sapiens)		100.0%
K7DNH8	ATP synthase subunit alpha (Pan troglodytes)		100.0%

b. *Homo sapiens* (human) or *Pan troglodytes* (chimpanzee); they are 100% identical.

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Human hemoglobin consists of four protein subunits: two from the alpha globin gene cluster (located on chromosome 16) and two more from the beta globin gene cluster (located on chromosome 11). But there are at least nine different globin genes in these clusters, which are: zeta, mu, alpha, theta1, epsilon, gamma1, gamma2, delta and beta. Use the proteins in "*file3.fasta*" (https://cbdm.uni-mainz.de/mb18/).

a. Sort them either in cluster alpha or cluster beta.
Alpha: zeta, mu, alpha, theta1. Beta: epsilon, gamma1, gamma2, delta and beta.

b. Why do you think they are clustered in either cluster alpha or cluster beta?
Paralogous expansion from one ancestral alpha and one ancestral beta.

Your list:...ITXRE	Entry	Entry name		Protein names
HBAZ_HUMAN	P02008	HBAZ_HUMAN		**Hemoglobin subunit zeta**
HBM_HUMAN	Q6B0K9	HBM_HUMAN		**Hemoglobin subunit mu**
HBA_HUMAN	P69905	HBA_HUMAN		**Hemoglobin subunit alpha**
HBAT_HUMAN	P09105	HBAT_HUMAN		**Hemoglobin subunit theta-1**
HBE_HUMAN	P02100	HBE_HUMAN		**Hemoglobin subunit epsilon**
HBG1_HUMAN	P69891	HBG1_HUMAN		**Hemoglobin subunit gamma-1**
HBG2_HUMAN	P69892	HBG2_HUMAN		**Hemoglobin subunit gamma-2**
HBD_HUMAN	P02042	HBD_HUMAN		**Hemoglobin subunit delta**
HBB_HUMAN	P68871	HBB_HUMAN		**Hemoglobin subunit beta**

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Phylogeny

*Images from: UniProt, Trex, UCSC

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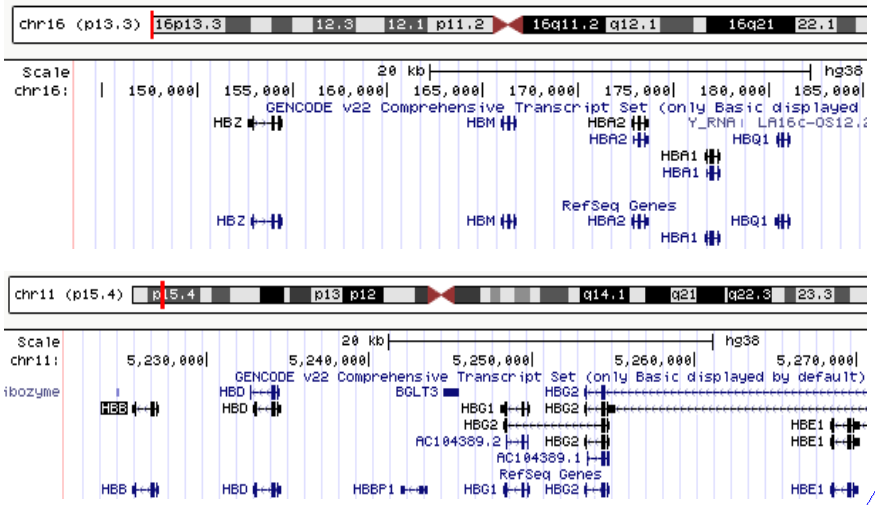
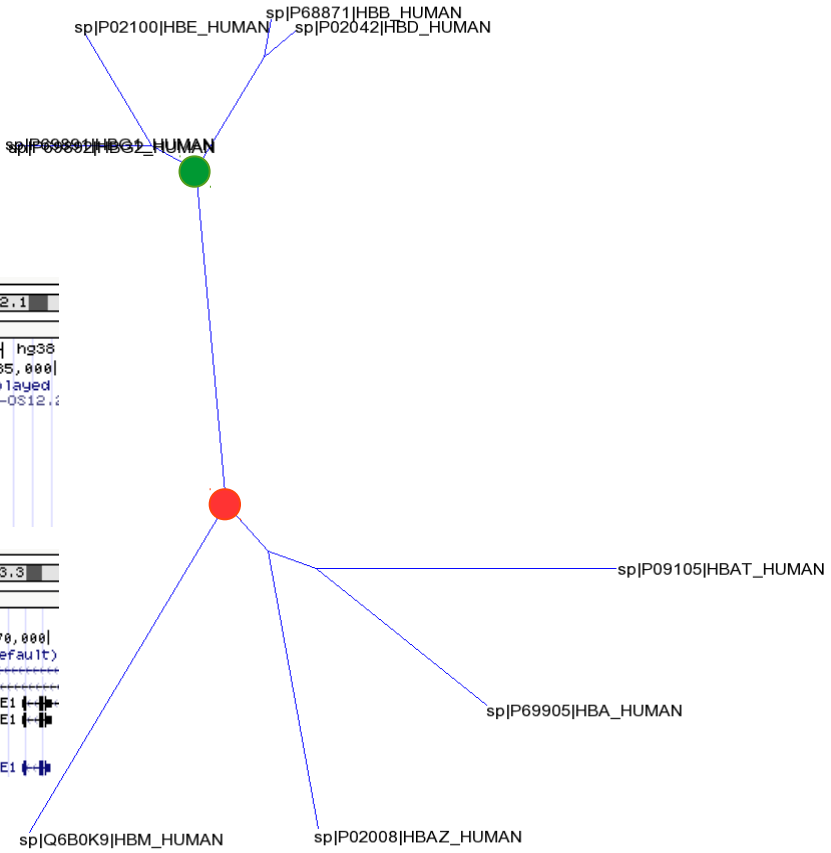
Your list:...ITXRE	Entry	Entry name		Protein names
HBAZ_HUMAN	P02008	HBAZ_HUMAN		Hemoglobin subunit zeta
HBM_HUMAN	Q6B0K9	HBM_HUMAN		Hemoglobin subunit mu
HBA_HUMAN	P69905	HBA_HUMAN		Hemoglobin subunit alpha
HBAT_HUMAN	P09105	HBAT_HUMAN		Hemoglobin subunit theta-1
HBE_HUMAN	P02100	HBE_HUMAN		Hemoglobin subunit epsilon
HBG1_HUMAN	P69891	HBG1_HUMAN		Hemoglobin subunit gamma-1
HBG2_HUMAN	P69892	HBG2_HUMAN		Hemoglobin subunit gamma-2
HBD_HUMAN	P02042	HBD_HUMAN		Hemoglobin subunit delta
HBB_HUMAN	P68871	HBB_HUMAN		Hemoglobin subunit beta

a. Using Trex:

Cluster alpha

Cluster beta





b. Paralogous expansion from one ancestral alpha and one ancestral beta.

*Images from: Wikipedia

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Consider the following sequences: Q9T4B2 (CYB_DELDE, dolphin), P00156 (CYB_HUMAN, human), P00157 (CYB_BOVIN, cattle), Q9MIX8 (CYB_DANRE, zebra fish), P18946 (CYB_CHICK, chicken), Q36461 (CYB_ORNAN, platypus) and P00160 (CYB_XENLA, frog).

Do you think that a phylogenetic tree built using these sequences would be coherent with evolution? Check with the taxonomy provided by UniProt (http://www.uniprot.org/taxonomy/).

Human
(*Homo sapiens*)

Dolphin
(*Delphinus delphis*)

Cattle
(*Bos taurus*)

Chicken (rooster)
(*Gallus gallus*)

Zebra fish
(*Danio rerio*)

Platypus
(*Ornithorhynchus anatinus*)

Frog
(*Xenopus laevis*)

Phylogeny

*Images from: UniProt, Trex

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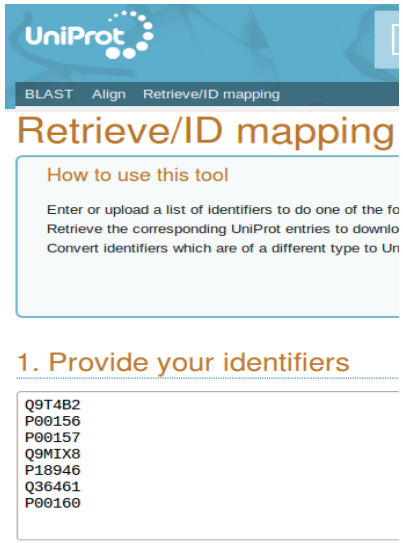
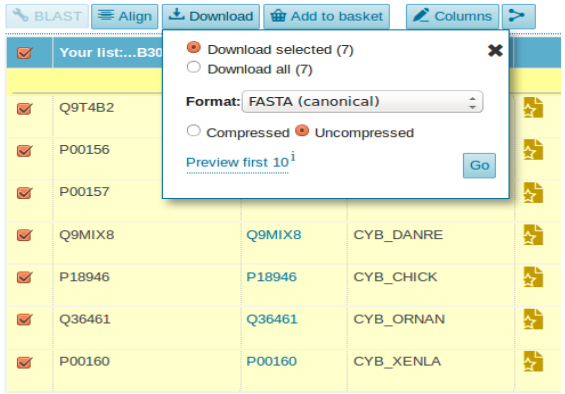
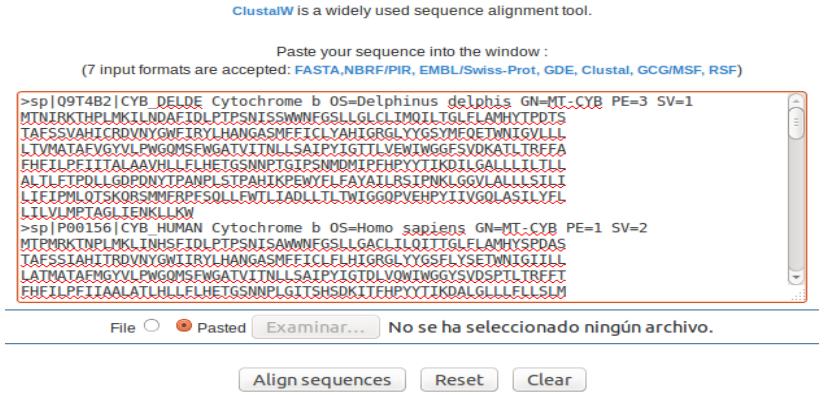
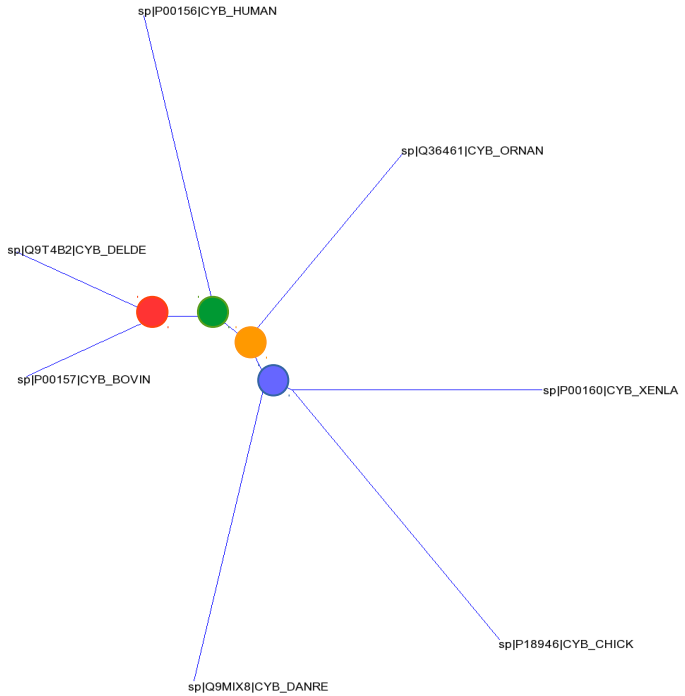






Dolphin → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Eutheria › Laurasiatheria › Cetartiodactyla › Cetacea › Odontoceti › Delphinidae › Delphinus
Cattle → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Eutheria › Laurasiatheria › Cetartiodactyla › Ruminantia › Pecora › Bovidae › Bovinae › Bos
Human → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Eutheria › Euarchontoglires › Primates › Haplorrhini › Catarrhini › Hominidae › Homo
Platypus → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Mammalia › Monotremata › Ornithorhynchidae › Ornithorhynchus
Frog → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Amphibia › Batrachia › Anura › Pipoidea › Pipidae › Xenopodinae › Xenopus › Xenopus
Chicken → Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Archelosauria › Archosauria › Dinosauria › Saurischia › Theropoda › Coelurosauria › Aves › … > Gallus
Zebrafish →Eukaryota › Metazoa › Chordata › Craniata › Vertebrata › Euteleostomi › Actinopterygii › Neopterygii › Teleostei › Ostariophysi › Cypriniformes › Cyprinidae › Danio



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Consider the following sequences: P50225, P50226, P0DMM9, P0DMN0, O43704, O00338, Q6IMI6, O75897. All of them are part of a human paralog family (sulfotransferases).

a. Look for the coordinates of the substrate binding region in the UniProt entry "P50225". Do you expect all the paralogs to share this substrate binding region? Why? Check it.
Yes, because they share the motif "K[ST]H".

b. Using the previous sequences, could you determine which human paralog is the ortholog of the sequence in "*file4.fasta*" (https://cbdm.uni-mainz.de/mb18/)? Do not use BLAST.
The ortholog of "protein_of_interest" is ST1B1_HUMAN.

c. Which protein is the one found in "*file4.fasta*"?
ST1B1_CANLF, from *Canis familiaris* (dog).

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MSA + Phylogeny + Homology

*Images from: UniProt, Trex

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(P50225)

Feature key	Position(s)	Length	Description
Region [i]	106 – 108	3	Substrate binding

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        10         20         30         40         50
MELIQDTSRP PLEYVKGVPL IKYFAEALGP LQSFQARPDD LLISTYPKSG
        60         70         80         90        100
TTWVSQILDM IYQGGDLEKC HRAPIFMRVP FLEFKAPGIP SGMETLKDTP
       110        120        130        140        150
APRLLKTHLP LALLPQTLLD QKVKVVYVAR NAKDVAVSYY HFYHMAKVHP
       160        170        180        190        200
EPGTWDSFLE KFMVGEVSYG SWYQHVQEWW ELSRTHPVLY LFYEDMKENP
       210        220        230        240        250
KREIQKILEF VGRSLPEETV DFVVQHTSFK EMKKNPMTNY TTVPQEFMDH
       260        270        280        290
SISPFMRKGM AGDWKTTFTV AQNERFDADY AEKMAGCSLS FRSEL
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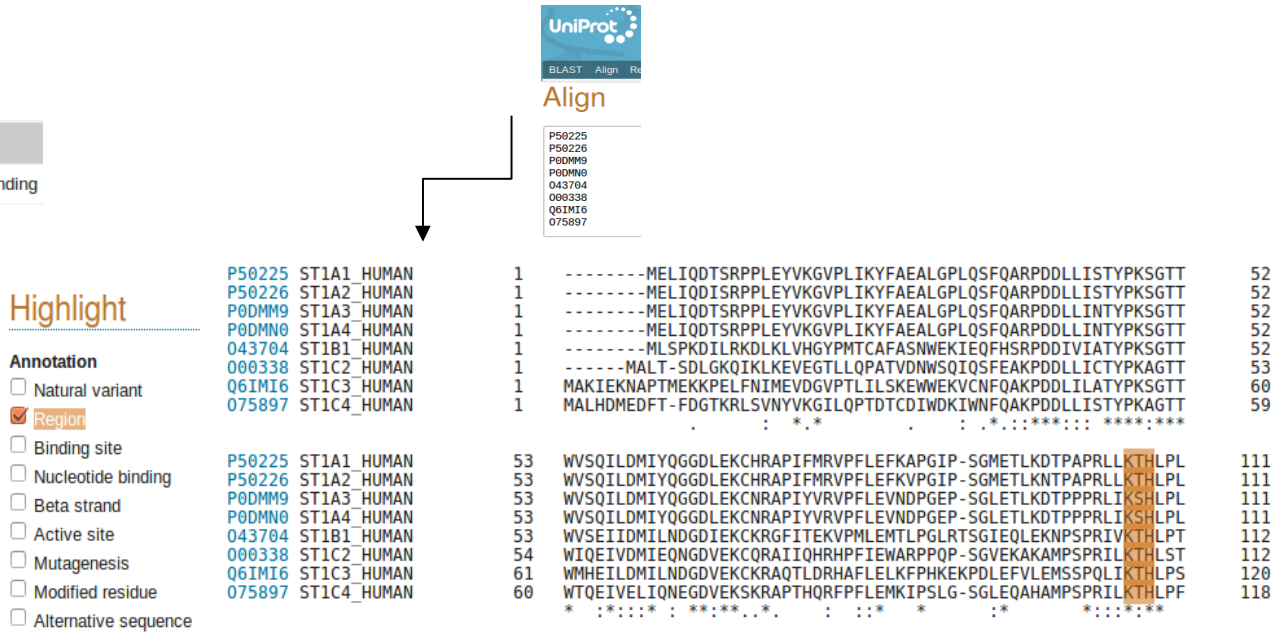
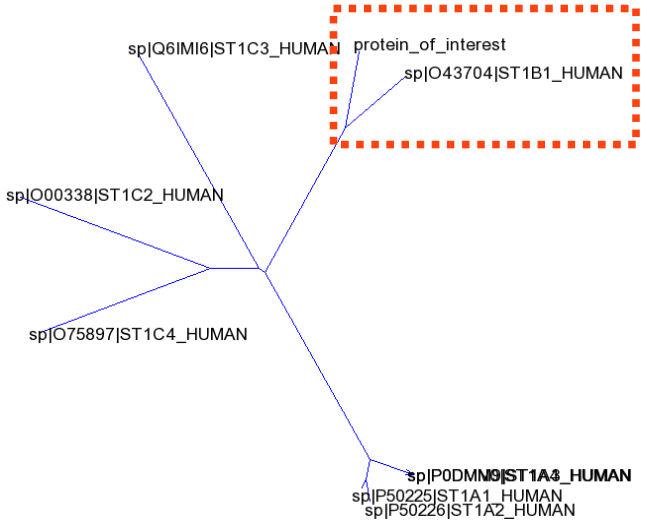


a. Yes, because they share the motif “K[ST]H”.

b. The ortholog of “protein_of_interest” is ST1B1_HUMAN.

c. ST1B1_CANLF, from *Canis familiaris* (dog).

Entry	Protein names	Match hit (200 400 600 800 1k)	Identity
Q95JD5	Sulfotransferase family cytosolic 1B member 1 (Canis lupus familiaris)		100.0%
F6V3V8	Sulfotransferase (Canis lupus familiaris)		98.3%
D2I2Q5	Sulfotransferase (Ailuropoda melanoleuca)		94.3%
U6CQE2	Sulfotransferase (Neovison vison)		93.6%



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