
Master Biomedizin 2021

- 1) UniProt
- 2) Homology
- 3) MSA
- 4) Phylogeny

1

- a. What is the AC of the UniProt entry for the human insulin?
- b. How many isoforms for this protein are described in that entry?
- c. How many times has this entry been modified?
... and the protein sequence?
- d. With how many proteins does the human insulin interact?

Homology

2

Classify the following protein pairs based on their evolutionary relationship.
Note: proteins A and B have a common ancestor.

a. Protein A mouse / Protein A human →

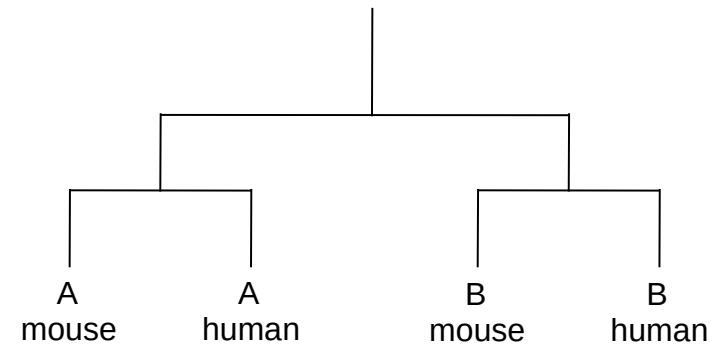
b. Protein A mouse / Protein B mouse →

c. Protein A mouse / Protein B human →

d. Protein A human / Protein B mouse →

e. Protein A human / Protein B human →

f. Protein B mouse / Protein B human →



3

- a. Using the human protein “P21741”, find its orthologous proteins in frog (*Xenopus laevis*) and get their UniProt AC.
- b. Check the identity between the orthologs (human – frog proteins).
- c. Check the identity between the paralogs (frog – frog proteins).



Human
(*Homo sapiens*)



Frog
(*Xenopus laevis*)

4

- a. Based on the sequence of the “ATP synthase subunit a” protein from the extinct mammoth (*Mammuthus primigenius*), was the mammoth closer to the asian elephant (*Elephas maximus*) or to the african elephant (*Loxodonta africana*)? Use only SwissProt proteins.
- b. Is there evidence enough to conclude if they are / are not closer?
- c. Could you check with the “cytochrome b” protein too? Use only SwissProt proteins.



Woolly mammoth
(*Mammuthus primigenius*)



Asian elephant
(*Elephas maximus*)



African elephant
(*Loxodonta africana*)

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- a. Based solely on the sequence of the “Cytochrome b” protein (Q8SG72) from the extinct dodo (*Raphus cucullatus*), was the dodo closer to the Nicobar pigeon “*Caloenas nicobarica*” or to the chicken (*Gallus gallus*)? Use NCBI Blast.
- b. There are more than 300 species of pigeons. Do the results differ if you consider the street pigeon (*Columba livia*)?



Dodo
(*Raphus cucullatus*)



Nicobar pigeon
(*Caloenas nicobarica*)



Chicken (rooster)
(*Gallus gallus*)



Pigeon
(*Columba livia*)

6

- a.** The UniProt entry “P04585” contains the Gag-Pol polyprotein from the virus HV1H2. Do you think it would resemble any protein in the human proteome (*Homo sapiens*)? Check it using NCBI Blast.
- b.** The Gag-Pol polyprotein is composed of many proteins. Using only protein entries from *Chlamydia trachomatis*, can you identify some of the individual proteins of the Gag-Pol polyprotein?

MSA

7

Given the following alignments,

classify them in:

- Pairwise / multiple
- Local / global

calculate their:

- % similarity
- % identity

```
>Protein_A  
KKKYYWKKT  
>Protein_B  
AKKYYW  
>Protein_C  
RKRWWWRT
```

a) Protein_A YYWW
Protein_B YYWW

b) Protein_A KKKYYWKKT
Protein_B AKKYYW---

c) Protein_A KKKYYWKKT
Protein_B AKKYYW---
Protein_C AKRWWWRT
*:::**

8

- a. The proteins “P11582” and “P02226” are paralogs, but they differ in length (152 vs 161 amino acids). Is there an extra region in P02226, or the extra amino acids are dispersed along the protein? Use UniProt.
- b. How could that have happened in evolution?
- c. If you blast P02226 and use only SwissProt proteins as database, how many results do you get? Is this protein present in any bacterial proteome?

// FYI: Protein entry P02226 is one of the oldest in SwissProt; check the date!

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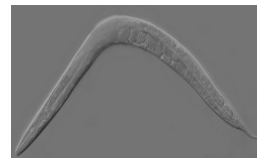
- a. Both “P17861” (XBP1_HUMAN) and “Q3SZZ2” (XBP1_BOVIN) are “X-box binding protein 1” proteins. Can you detect which region/s of these proteins is/are important for their function? Why? Use Clustal Omega. What should you do to detect them?
- b. Add the proteins “G5EE07” (G5EE07_CAEEL) and “Q8UVQ5” (Q8UVQ5_DANRE) to the study. Are you able to identify that region/s now? Why? Use Clustal Omega.
- c. Check the positional annotations in the entry of the human protein. Was the region you identified annotated as a domain?



Human
(*Homo sapiens*)



Cattle
(*Bos taurus*)



Worm
(*Caenorhabditis elegans*)



Zebra fish
(*Danio rerio*)

10

a. Using the following set of orthologous proteins, predict which regions are important for their function. Use T-Coffee.

Q90WY9
P97801
Q98SU9
Q9W6S8
W4XFQ6
A0A088A467

b. Check your predictions in their UniProt entries.

11

a. Using the following set of orthologous proteins, do you think the evolution is pressuring them? Use UniProt.

Q02078
Q5REW7
Q2MJT0
Q60929
A2VDZ3
A2ICN5
Q9W6U8

b. Have they evolved? Did they gain or lose any domain/motif/region?

Phylogeny

12

A patient comes to the hospital. He was just bitten by a snake. We have the sequence of the mitochondrial gene ND4 of 24 species of snake ("*snakes.fasta*"; <https://cbdm.uni-mainz.de/mb21/>). We have three antidotes available. Given the following information, which antidote would you administer the patient?

- 1) The snake that bit the patient is in terrarium #1.
- 2) The most distant snake species is in terrarium #12.
- 3) Antidote1 is indicated against bites from the species in terrarium #3.
- 4) Antidote2 is indicated against bites from the species in terrarium #11.
- 5) Antidote3 is indicated against bites from the species in terrarium #17.
- 6) Snakes in terrariums #15 and #20 are non-venomous.



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- a. All of the sequences in “*file1.fasta*” (<https://cbdm.uni-mainz.de/mb21/>) are homologs. How many groups of orthologs would you say there are in this file? Use SeaView.

- b. What could you say about the history of this protein family?

- c. Would you say there is any wrongly annotated sequence?

14

- a. Using “*file2.fasta*” (<https://cbdm.uni-mainz.de/mb21/>), can you approximate to which taxonomic division belongs “proteinX”?
- b. From which organism could it be? After guessing, check it.

15

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/mb21/>), which includes an hemoglobin protein from *Gallus gallus* to be used as outgroup.

- a. Sort them either in cluster alpha or cluster beta.
- b. Why do you think they are clustered in either cluster alpha or cluster beta?

16

The sequences in “*file4.fasta*” (<https://cbdm.uni-mainz.de/mb21/>) are orthologs from dolphin, human, cattle, zebra fish, chicken, platypus and frog.

- a. Build a phylogenetic tree using these sequences.
- b. Check in UniProt > Taxonomy (<https://www.uniprot.org/taxonomy/>) if the phylogenetic tree built only from that one protein family is coherent with evolution.