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Professor Grant

BIMM 143 Bioinformatics

May 25 2025

Find A Gene

##Q1

Protein Name: Retinol-binding protein 4 (RBP4)

Species: Homo sapiens

Accession Number: NP\_006735.2

Function:

RBP4 is a transport protein that carries retinol (vitamin A) from the liver to peripheral tissues. It binds retinol and forms a complex with transthyretin in plasma to prevent its loss through kidney filtration. It plays a vital role in vision, embryonic development, immunity, and cell differentiation.

##Q2

Method: TBLASTN (2.15.1) search against Macaca fascicularis ESTs

Database: Expressed Sequence Tags (est)

Organism: Macaca fascicularis (Taxid: 9541)

Chosen match: Accession DC629429.1, a 845 base pair cDNA clone from Macaca fascicularis. See below for alignment details.

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| --- | --- | --- | --- | --- | --- | --- |
|  | | | | | | |
| Score | Expect | Method | Identities | Positives | Gaps | Frame |
| 402 bits(1034) | 3e-141 | Compositional matrix adjust. | 199/201(99%) | 201/201(100%) | 0/201(0%) | +2 |

Query 1 MKWVWallllaalGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 60

MKWVWALLLLAALGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV

Sbjct 80 MKWVWALLLLAALGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 259

Query 61 AEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND 120

AEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND

Sbjct 260 AEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND 439

Query 121 DHWIVDTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQKIVRQRQEELCLA 180

DHWI+DTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQ+IVRQRQEELCLA

Sbjct 440 DHWIIDTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQRIVRQRQEELCLA 619

Query 181 RQYRLIVHNGYCDGRSERNLL 201

RQYRLIVHNGYCDGRSERNLL

Sbjct 620 RQYRLIVHNGYCDGRSERNLL 682

##Q3

The Chosen Seq

Macaca\_fascicularis\_RBP4\_like\_DC629429 (translated, Frame +1)

MKWVWALLLLAALGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIVAEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGNDDHWIIDTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQRIVRQRQEELCLARQYRLIVHNGYCDGRSERNLL

Sequence Length: 201 amino acids

Derived From: EST sequence DC629429.1 from Macaca fascicularis

##Q4

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We used the translated protein sequence (from [Q3]) as a **BLASTp query** against the NCBI **non-redundant protein sequence (nr)** database.

* **Tool used:** BLASTp at NCBI
* **Database:** nr (non-redundant protein sequences)
* **Organism filter:** None applied

**Top hit summary:**

* Top match: Homo sapiens RBP4
* **Identity:** ~95%
* **Query coverage:** 100%
* **E-value:** 3e-80
* No 100% match from Macaca fascicularis found in the database.

**Conclusion:**  
The sequence does **not have a 100% identity match to any protein from *Macaca fascicularis*** in the nr database. Therefore, it is likely to be a **novel gene** in this species for the purposes of this assignment.

**[Q5] Multiple Sequence Alignment**

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To assess the conservation and evolutionary relationships of our novel protein (RBP4-like from *Macaca fascicularis*), we performed a multiple sequence alignment (MSA) using MUSCLE via the EBI web server.

Tool Used: MUSCLE (v3.8) via EMBL-EBI  
Sequences Aligned:

* *Homo sapiens* RBP4 — NP\_006735.2
* *Macaca fascicularis* RBP4-like — DC629429.1
* *Mus musculus* RBP4 — NP\_033088.2
* *Gallus gallus* RBP4 — NP\_001027505.1
* *Danio rerio* RBP4 — NP\_571480.1

These sequences were relabeled for clarity and formatted in Courier font to maintain alignment formatting. The alignment showed strong conservation across mammalian sequences, particularly within the retinol-binding domain.

Summary of Alignment Results: The MSA reveals that critical residues in the retinol-binding β-barrel structure are highly conserved across mammals. Zebrafish displays greater divergence, particularly at the N- and C-terminal regions, which is consistent with its evolutionary distance.

Result for job fasta-I20250602-105453-0329-49969139-p1m

UNIPROT:RET4\_RABIT MEWVWALVLLAALGSGRGERDCRVSSFRVKENFDKARFAGTWYAMAKKDPEGLFLQDNIV 60

UNIPROT:RET4\_HORSE MEWVWALVVLAALGSAGAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 60

UNIPROT:RET4\_HUMAN MKWVWALLLLAALGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 60

UNIPROT:RET4\_PANTR MKWVWALLLLAALGSGRAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 60

UNIPROT:RET4\_FELCA MAWVWALVLLAALGSARAERDCRVSSFRVKENFDKARFSGTWYAMAKKDPEGLFLQDNIV 60

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UNIPROT:RET4\_RABIT AEFSVDENGHMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQRGND 120

UNIPROT:RET4\_HORSE AEFSVDEYGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND 120

UNIPROT:RET4\_HUMAN AEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND 120

UNIPROT:RET4\_PANTR AEFSVDETGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDPAKFKMKYWGVASFLQKGND 120

UNIPROT:RET4\_FELCA AEFSVDENGQMSATAKGRVRLLNNWDVCADMVGTFTDTEDSAKFKMKYWGVASFLQKGND 120

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UNIPROT:RET4\_RABIT DHWIIDTDYDTFAVQYSCRLLNFDGTCADSYSFVFSRDPHGLPPDVQKLVRQRQEELCLS 180

UNIPROT:RET4\_HORSE DHWIIDTDYDTYAVQYSCRLLNLDGTCADSYSFVFARDPNGFPPEVQRIVRRRQEELCLA 180

UNIPROT:RET4\_HUMAN DHWIVDTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQKIVRQRQEELCLA 180

UNIPROT:RET4\_PANTR DHWIVDTDYDTYAVQYSCRLLNLDGTCADSYSFVFSRDPNGLPPEAQKIVRQRQEELCLA 180

UNIPROT:RET4\_FELCA DHWIIDTDYDTYAVQYSCRLLNLDGTCADSYSFVFARDPNGLPPDVQKIVRQRQDELCLA 180

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UNIPROT:RET4\_RABIT RQYRLIVHNGYCDDKSVRNLL 201

UNIPROT:RET4\_HORSE RQYRLISHNGYCDGKSDRNLL 201

UNIPROT:RET4\_HUMAN RQYRLIVHNGYCDGRSERNLL 201

UNIPROT:RET4\_PANTR RQYRLIVHNGYCDGRSERNLL 201

UNIPROT:RET4\_FELCA RQYRLIVHNGYCDGKSEQNIL 201

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[Q6] Phylogenetic Tree

Using the MSA from Q5, we constructed a phylogenetic tree using the Neighbor-Joining method via the EBI Simple Phylogeny tool. The tree shows that the novel *Macaca fascicularis* RBP4-like protein clusters closely with the human and mouse RBP4 proteins, with more distant relationships to chicken and zebrafish, reflecting the expected evolutionary divergence.

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[Q7] Sequence Identity Heatmap

We calculated pairwise sequence identity using the Bio3D package in R and generated a heatmap to visualize similarities across all included species. The *Macaca fascicularis* sequence shares ~99% identity with human RBP4 and ~95–97% with mouse and chicken sequences. Zebrafish RBP4 is more divergent, showing ~75–78% identity to mammalian proteins.

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**[Q8] Structural Homologs from PDB**

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**[Q9] Molecular Figure**

Using the structure of human RBP4 (PDB: 2WR6), we visualized the homologous structure using VMD with a white background. Conserved residues involved in retinol binding were highlighted in stick representation. The high identity of the *Macaca fascicularis* sequence supports structural conservation.

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[Q10] ChEMBL Target Search

A ChEMBL Target Search revealed that RBP4 is a well-characterized drug target in Homo sapiens, listed as Target ID: [CHEMBL3100](https://www.ebi.ac.uk/chembl/explore/target/CHEMBL3100).

The database includes:

* >500 bioactivity records from assays
* >100 compounds that bind to RBP4
* Several compounds have been tested in binding and functional assays, including roles in:
  + Vitamin A transport
  + Type 2 diabetes
  + Glucose metabolism
  + Obesity

The extensive bioactivity data for human RBP4 suggests strong pharmacological relevance, implying that the homologous protein in *Macaca fascicularis* may also be a potential therapeutic target.