Medical and Life Sciences (2026) 5(1): 01–21
ISSN (E): 2976-7245

Systems-Level Comparative Bioinformatics Analysis Of Liver-Associated Genes (ALB, TNF, F8, VDR, and FASN) Across Vertebrate Species

Mamoona Mushtaq[1]
Muhammad Asif Shabbir[2]
Fizza Shahid[3]
Ayesha Sattar[4]
Naureen Anwar[1]*

How to cite this article:
Mushtaq, M., Shabbir, M. A., Shahid, F., Sattar, A., & Anwar, N. (2026). Systems-level comparative bioinformatics analysis of liver-associated genes (ALB, TNF, F8, VDR, and FASN) across vertebrate species. *Medical and Life Sciences*, *5*(1), 1–21.
Received: 25 September 2025; Accepted: 27 December 2025; Published online: 23 February 2026

Abstract

The liver is a major metabolic organ that regulates nutrient homeostasis, immune response, coagulation, detoxification and endocrine function. For studying evolutionary conservation and structural-functional difference of vital hepatic genes among vertebrates, we undertook a comparative bioinformatics research on five major liver-associated genes (ALB, TNF, F8, VDR and FASN) in five species of vertebrates: *Homo sapiens, Bos taurus, Canis lupus familiaris, Mus musculus and Gallus gallus*. Nucleotide sequences were obtained from the NCBI database and aligned using MEGA 12 by ClustalW. Phylogenetic trees were generated with the Maximum likelihood method based on Tamura-Nei model. Amino acid sequences of proteins were translated by ExPASy Translate tool and confirmed by BLASTp homology search. Identification of conserved domains was performed with the NCBI CDD and comparisons to structures pooled to PDB templates. Phylogenetic separation among mammalian species was detected, since human, cow and dog formed closely related clusters and mouse had a moderate divergence with chicken as the farthest related species. ALB and FASN are the most conserved across species, indicating strong purifying selection for their metabolic roles. Contrastingly, TNF and F8 had more divergent sequences particularly in the avian, possibly representing lineage-specific adaptations in immune signaling or coagulation machinery. Conserved domain analysis verified the retention of conserved functional motifs such as ligand-binding sites, putative/receptor-interaction site interfaces, coagulation domains and catalytic regions for fatty acid synthesis. These results illustrate remarkable evolutionary conservation of liver-enriched functional genes among vertebrates and different divergence in species phylogeny and physiological adaptation. The work demonstrates the potential of cross-species in silico approaches to study functional conservation, comparative anatomy and use as a framework for translation and evolutionary studies in liver.

Keywords: Comparative genomics; Liver-associated genes; ALB; TNF; F8; VDR; FASN;

[1]Virtual University of Pakistan, Raiwind Road Campus, Lahore, Pakistan
Corresponding Author: naureen.anwar@vu.edu.pk
[2]College of Agriculture, University of Sargodha, Sargodha, Pakistan
[3]Allied Burn and Reconstructive Surgery Centre, Allied Hospital, Faisalabad, Pakistan
[4]University of Lahore, Sargodha, Pakistan

Phylogenetic analysis; Conserved domains; Vertebrate evolution; Bioinformatics; Protein structure analysis

1. Introduction

The liver is the largest glandular organ of the body with important functions in metabolism, detoxification, immune regulation and nutrient homeostasis (Alamri et al., 2018; Mohajan, 2025). It is a component of bile, metabolizes bilirubin and plays a role in lipid and glucose homeostasis, as well as the storage of vitamins and minerals to maintain whole-body homeostasis (Trefts & Gannon, 2017). The liver is involved not only in metabolic activities, but it also produces most of the circulating plasma proteins and plays a central role in osmotic pressure, coagulation cascades and energy homeostasis (Yosilia et al., 2024). Hepatic expression of various liver-expressed genes is required for these physiological processes. Albumin (ALB), the most abundant protein in plasma, is responsible for oncotic pressure maintenance and carries out hormone and metabolite transport functions (Spinella & Sahney et al., 2015). Tumor necrosis factor (TNF) is a central inflammatory mediator and immune modulator in hepatic stress or injury (Schwartz et al., 2020). Blood clotting depends on F8 and its deficiency leads to hemophilia A (Green, 2024; Gitschier et al., 1984), which occurs when it is largely synthesized by liver sinusoidal endothelial cells. A vitamin D receptor (VDR) is necessary for controlling transcriptional responses to maintenance of calcium and phosphate levels in the body (Bozic & Guzman, 2016). Fatty acid synthase (FASN) is a multifunctional protein that participates in fatty acid synthesis and acts an important regulator of lipid metabolism as well as energy homeostasis (Casado & Vallet, 1999; Singh et al., 2024).

The genes were isolated and characterized independently in different measurements related to metabolism, immunity or diseased state with limited cross-species comparative evolutionary analyses. Most of the previous work dealt with single-gene phylogenies or studies of function within particular biological systems (Metcalf et al., 2003; Vandepoele et al., 2024). The comparative context may, however, contribute to a deeper understanding of conserved functional domains, lineage-specific divergence and evolutionary adaptation across hepatic genes. Genomic comparisons can reveal how highly conserved liver-associated genes are between vertebrates despite the long divergence times (Bashir et al., 2025). It may be useful to elucidate functional limitations and discover structural stability in a variety of physiological systems to comprehend these patterns. Thus, the present work intends to compare the evolutionary and structural features of five liver-associated genes (ALB, TNF, F8, VDR and FASN) across five vertebrates: *Homo sapiens* (human), *Bos taurus* (cow), *Canis lupus* familiaris (dog), *Mus musculus* (mouse) and *Gallus gallus* (chicken) via sequence alignment, conserved domain identification, phylogenetic tree construction and protein structural comparison.

2. Materials and Methods

For analysis from five species of five different genera, protein coding genes encoding liver-specific metabolic function were selected. The chromosomal localization of these genes and their corresponding NC accession numbers presented in Table 1. NC accession numbers are unique values assigned by the NCBI RefSeq database that refer to particular DNA sequences (Cavusoglu et al., 2024). The purpose of this study is to establish evolutionary relationship among these five species in systematically scientific analysis with in-silico tools (Kabiraj et al., 2023).

2.1. Gene Selection

We identified 5 liver function genes based on their function in organ systems of 5 species. ALB maintains blood osmotic pressure. TNF is a key cytokine in the immune response. F8 is responsible for the synthesis of coagulation factor VIII, a major blood clotting protein. VDR controls calcium and phosphate homeostasis and vitamin D signal transmission (Nie et al., 2025). The FASN is a gene of lipid metabolism. These genes were chosen due to their crucial roles in homeostasis, immunity, coagulation and metabolism as well as adequate available genomic and proteomic data accessible in a variety of databases like NCBI and UniProt (Zhang et al., 2024).

2.2. Sequence Retrieval

Nucleotide sequences of the genes of interest were obtained in FASTA format from the NCBI website (Accessed in 2025). *Homo sapiens, Gallus gallus, Bos taurus, Canis lupus* familiaris and *Mus musculus* sequences were all extracted and filtered for further analysis. (Table 1).

Table 1. Genes in selected species with their reference sequence accession number.

Gene	Homo sapiens (Human)	Gallus gallus (Chicken)	Bos taurus (Cattle/Cow)	Mus musculus (House mouse)	Canis lupus familiaris (Domestic dog)
ALB (Albumin gene)	NC_000004.12 (73404287..73421482)	NC_052535.1 (50341494..50358196)	NC_037333.1 (88484961..88503330)	NC_000071.7 (90608729..90624461)	NC_051817.1 (62962229..62978876)
TNF (Tumor necrosis factor gene)	NC_000006.12 (31575565..31578336)	NC_052545.1 (925629..945258)	NC_037350.1 (27716170..27718943, complement)	NC_000083.7 (35418343..35420983, complement)	NC_051816.1 (1219807..1221672)
F8 (Coagulation factor gene)	NC_000023.11 (154835792..155022723, complement)	NC_052535.1 (2101058..2120537, complement)	NC_037357.1 (36013567..36155734)	NC_000086.8 (74213950..74426342, complement)	NC_051843.1 (126024520..126170925, complement)
VDR (Vitamin D receptor gene)	NC_000012.12 (47841537..47904994, complement)	NC_052565.1 (1098821..1128668, complement)	NC_037332.1 (32382453..32438249)	NC_000081.7 (97752308..97806177, complement)	NC_051831.1 (6920266..6976964)
FASN (Fatty acid synthase gene)	NC_000017.11 (82078338..82098236, complement)	NC_052549.1 (5537180..5573293)	NC_037346.1 (50776231..50794939)	NC_000077.7 (120696784..120715992, complement)	NC_051813.1 (826552..843813)

2.3. Multiple Sequence Alignment:

Sequence similarity search and conserved domain identification were performed using MEGA 12 software with multiple sequence alignment. Homologous regions were identified by aligning the nucleotide sequences with ClustalW (Wang et al., 2024).

2.4. Phylogenetic Analysis

Evolutionary relationships among genes were established using phylogenetic analysis. The phylogenetic trees based on aligned sequences were constructed by the Maximum Likelihood method as implemented in MEGA 12 using the Tamura-Nei model of nucleotide substitution. Tree topology reliability was evaluated using 1,000 bootstrap replicates.

2.5. Protein Translation

Nucleotide sequences were translated into amino acid sequences using the ExPASy Translate Tool. Translated protein sequences were blasted using NCBI BLASTp in order to check the accuracy of translation, and confirmed that these sequences corresponded with the query and/or analogous hits. Homology Validation: The 5 sequences of the first five genes, each translated amino acid at a time from the five species, were combined to yield one phylogenetic tree. Protein sequence alignment and tree operations were performed in MEGA 12 to interrogate the structural and functional conservation of the protein type. Conserved Domain Analysis: Conserved domains in the translated protein sequences were determined by NCBI CDD and CD-search Tool. Functionally relevant motifs which are related to the biological functions of these genes were identified.

2.6. Functional Clustering

The comparative protein structural analysis was conducted by using available three-dimensional structures from the Protein Data Bank (PDB). The sequences of translated genes were aligned with the available structural templates to determine conserved domain architecture.

2.7. Structural Modeling:

Finally, comparative analysis of nucleotide sequences, protein alignments, conserved domains and structural features of the five genes was conducted across the five species.

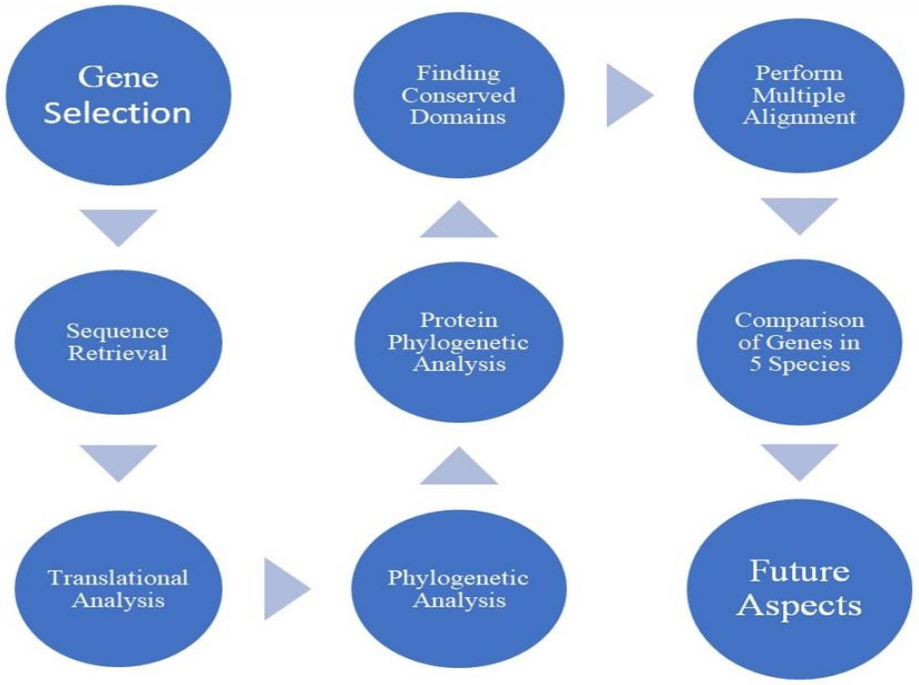

Figure 1. Flow chart exhibiting the overall bioinformatic workflow

3. Results

Although structurally conserved domains were generally preserved across species, significant differences in loop areas, especially in TNF and VDR, may influence receptor-binding affinities and regulatory interactions (Schwartz et al., 2020; Ramagopalan et al., 1999). Multiple Sequence

3.1. Alignment and Conserved Domains:

To identify conserved nucleotide blocks, multiple sequence alignment was performed in MEGA 12 and ClustalW. Mammalian sequences from all five genes were found to be highly conserved, as per the findings, with ALB, FASN and F8 being the most similar. Avian evolution revealed pathways through the significant divergence of chicken F8 and FASN sequences. Conserved blocks were particularly evident in gene-coding regions indicating functionally significant regions (Figure 2A, B, C, D and E).

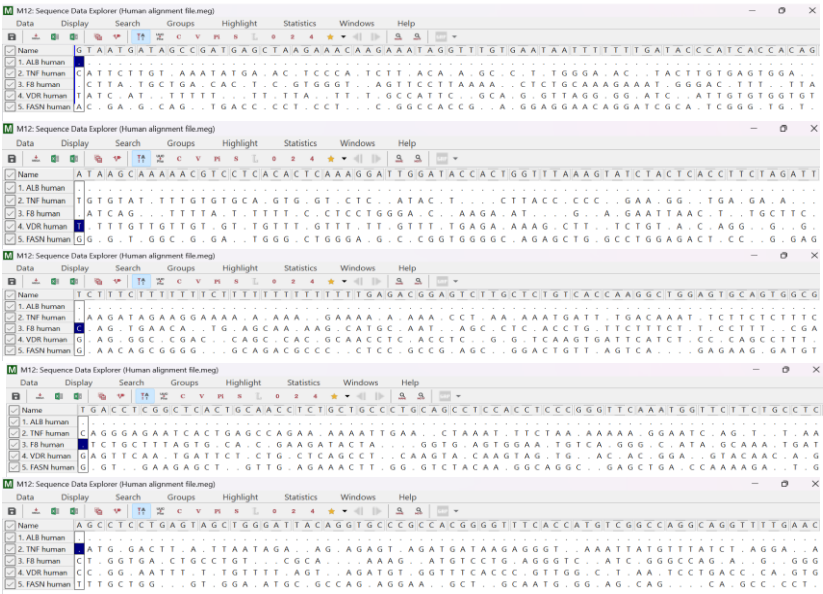

Figure 2A: Multiple sequence alignment of selected liver-related gene nucleotide sequences (ALB, TNF, F8, VDR and FASN) in human using MEGA 12 software to identify conserved regions

Figure 2B. Multiple sequence alignment of selected liver-related gene nucleotide sequences (ALB, TNF, F8, VDR and FASN) in chicken using MEGA 12 software to identify conserved regions.

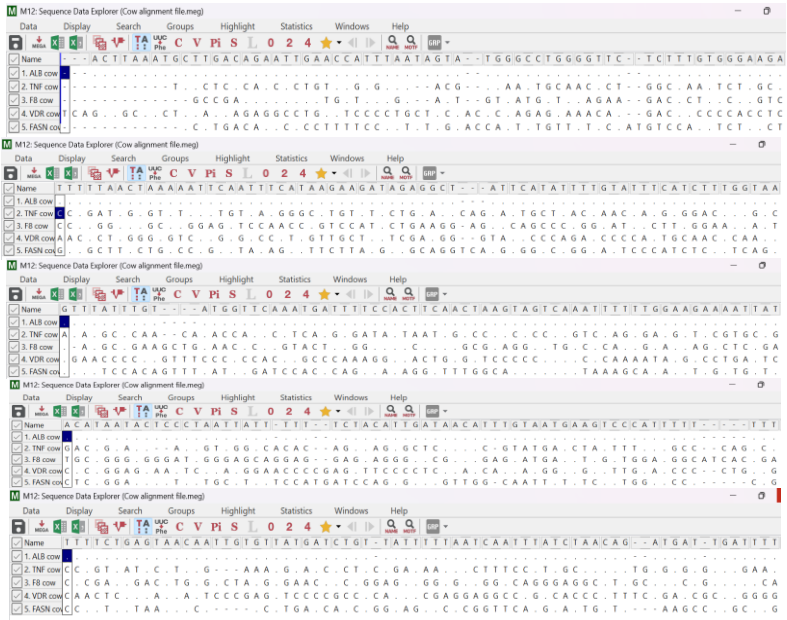

Figure 2C. Multiple sequence alignment of selected liver-related gene nucleotide sequences (ALB, TNF, F8, VDR and FASN) in the cow using MEGA 12 software to identify conserved regions.

Figure 2D. Multiple sequence alignment of selected liver-related gene nucleotide sequences (ALB, TNF, F8, VDR and FASN) in the house mouse using MEGA 12 software to identify conserved regions.

Figure 2E. Multiple sequence alignment of selected liver-related gene nucleotide sequences (ALB, TNF, F8, VDR and FASN) in the dog using MEGA 12 software to identify conserved regions.

3.2. Conserved Domain Analysis

Conserved domain predictions were performed against the NCBI Conserved Domain Database (CDD). Conserved motifs that corresponded to known gene functions were found. ALB possessed albumin-binding domains essential for ligand transport. TNF identified conserved cytokine receptor-binding domains involved in immune signaling. F8 found domains necessary for blood coagulation and interaction with von Willebrand factor. VDR showed nuclear receptor ligand-binding domains that mediate transcriptional regulation. FASN possessed complex multi-enzymatic domains for fatty acid synthesis. These regions were well conserved across mammals, whereas limited sequence variation in chicken reflected evolutionary divergence of some motifs, particularly TNF and FASN (Figure 3A, B, C, D and E).

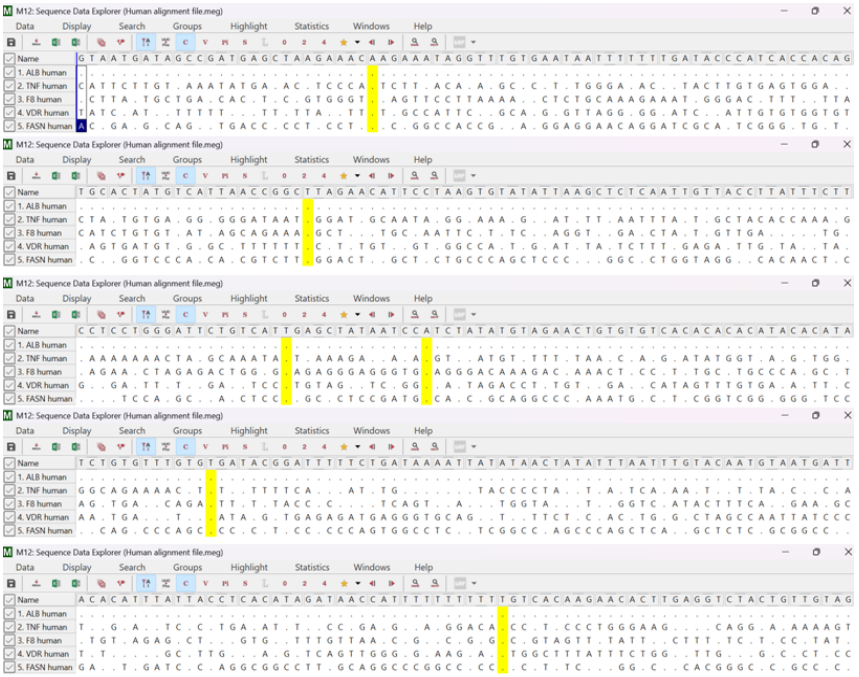

Figure 3A. The high-resolution figure of gene sequences is arranged to show the regions of high conservation in the selected human genes.

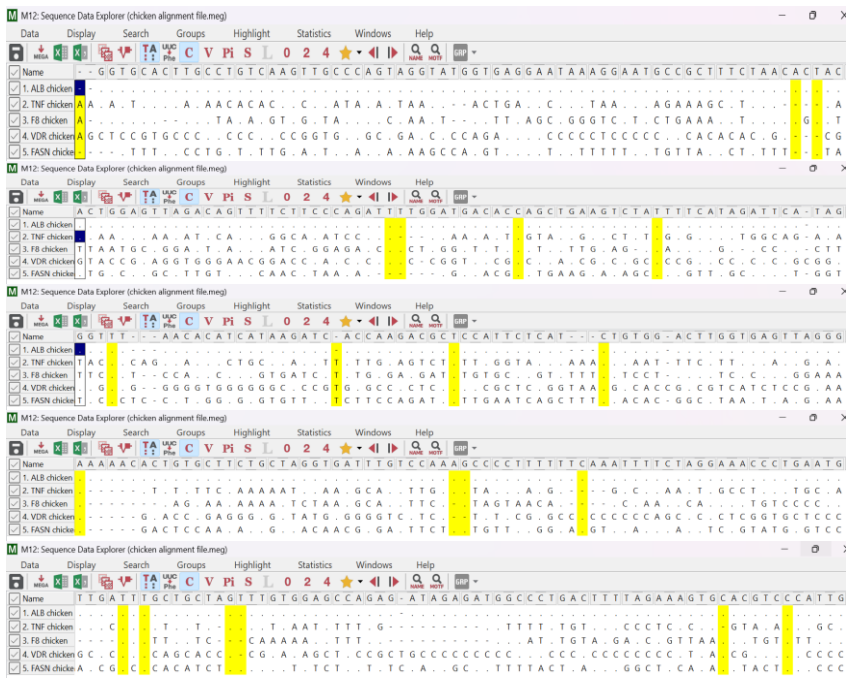

Figure 3B. The high-resolution figure of gene sequences arranged, showing the regions of high conservation in the selected genes in the chicken.

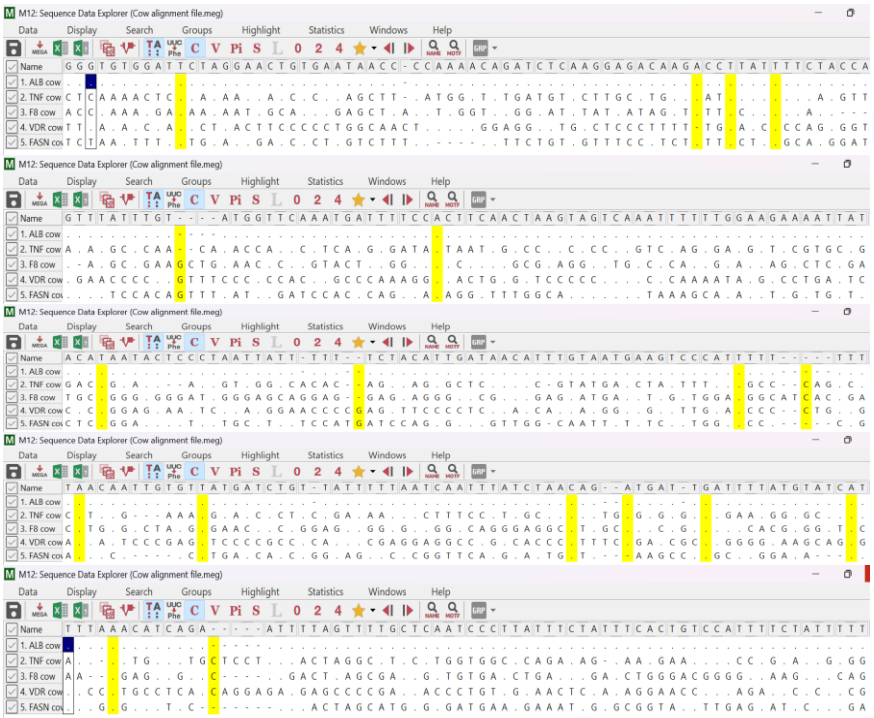

Figure 3C. The high-resolution figure of gene sequences arranged, showing the regions of high conservation in the selected genes in the cow.

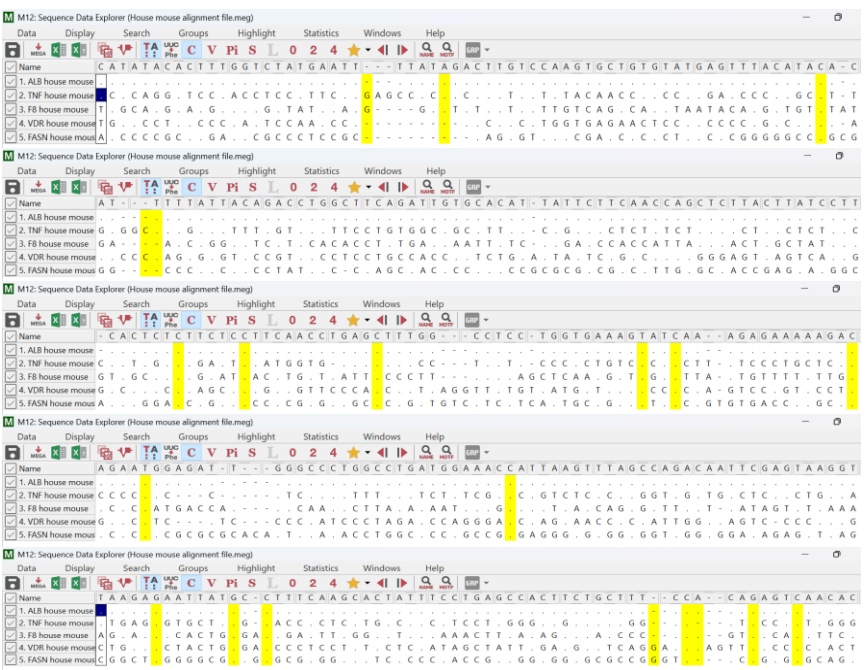

Figure 3D. The high-resolution figure of gene sequences arranged, showing the regions of high conservation in the selected genes in the house mouse.

Figure 3E. The high-resolution figure of gene sequences arranged, showing the regions of high conservation in the selected genes in the dog.

3.3. Protein Translation and Verification

The ExPASy Translate tool was also used to translate nucleotide sequences into amino acid sequences. BLASTp, used to identify the protein based on high homology between human, cow and dog sequences, was employed. Chicken proteins had lower similarity scores, reflecting evolutionary distance, while mammalian proteins showed over 85% sequence identity in the majority of genes (Figure 4A, B, C, D and E).

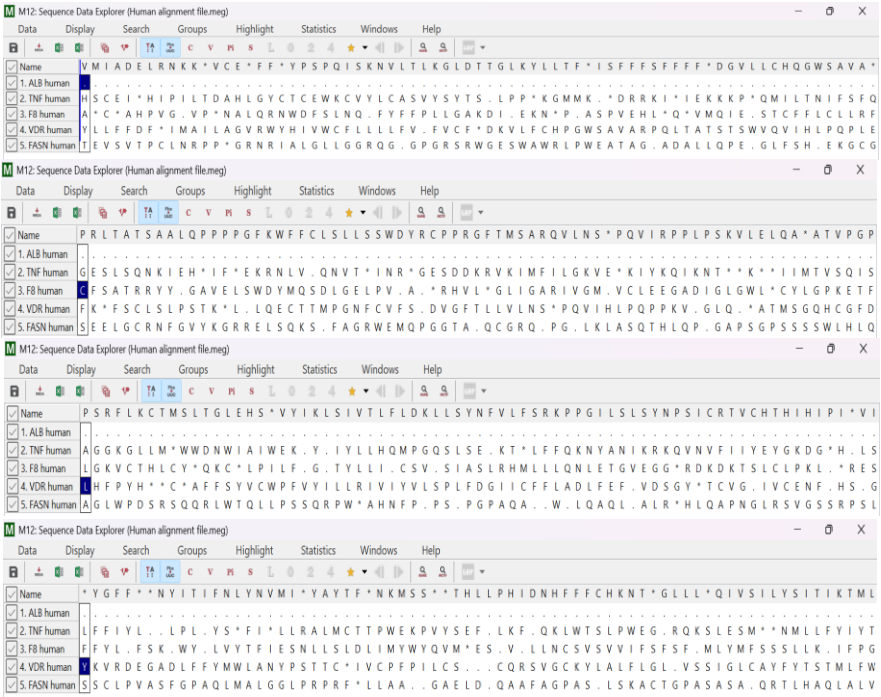

Figure 4A. Translated protein sequences of selected human genes, displayed using ExPASy Translate, showing the resulting amino acid chains.

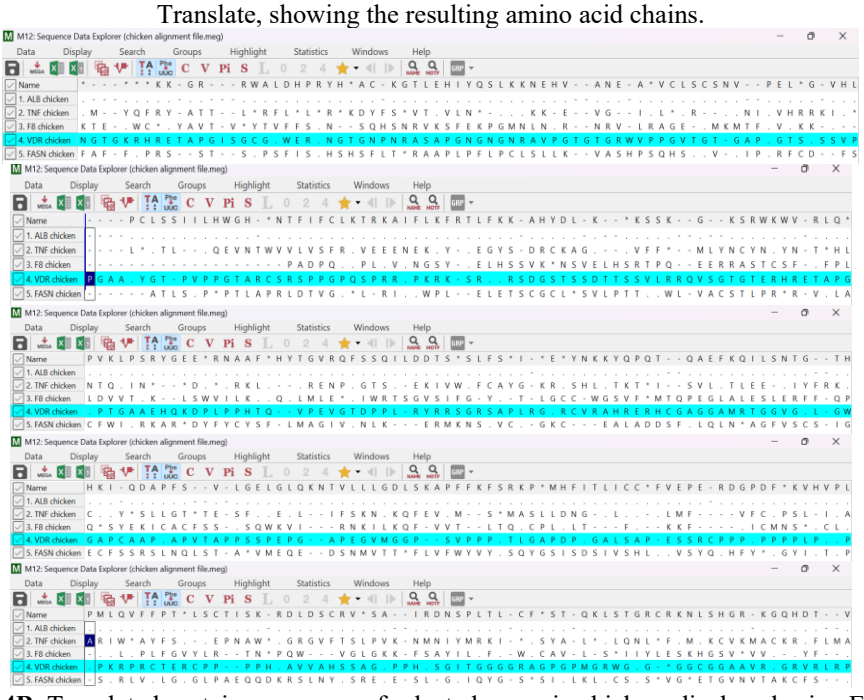

Figure 4B. Translated protein sequences of selected genes in chicken, displayed using ExPASy Translate, showing the resulting amino acid chains.

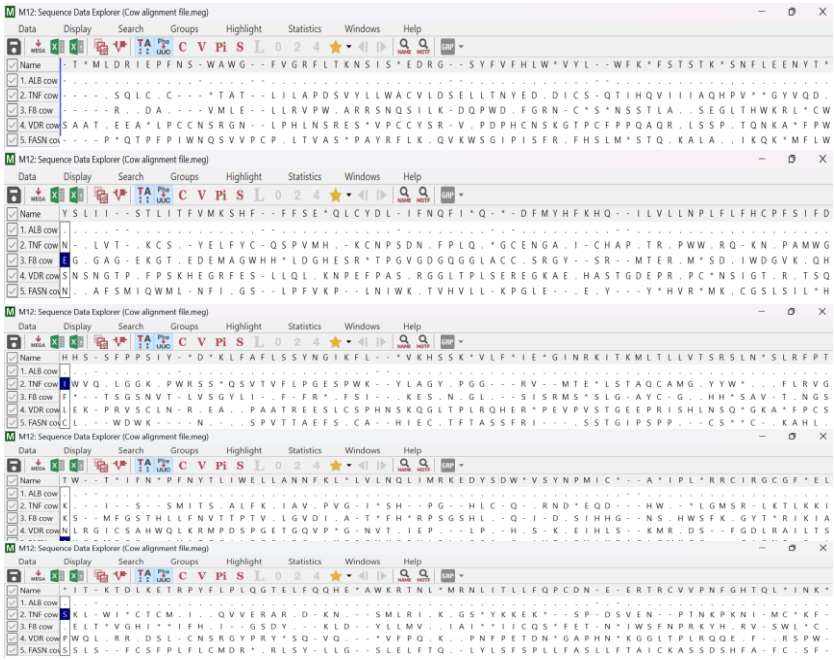

Figure 4C. Translated protein sequence of selected genes in the cow, displayed using ExPASy Translate, showing the resulting amino acid chains.

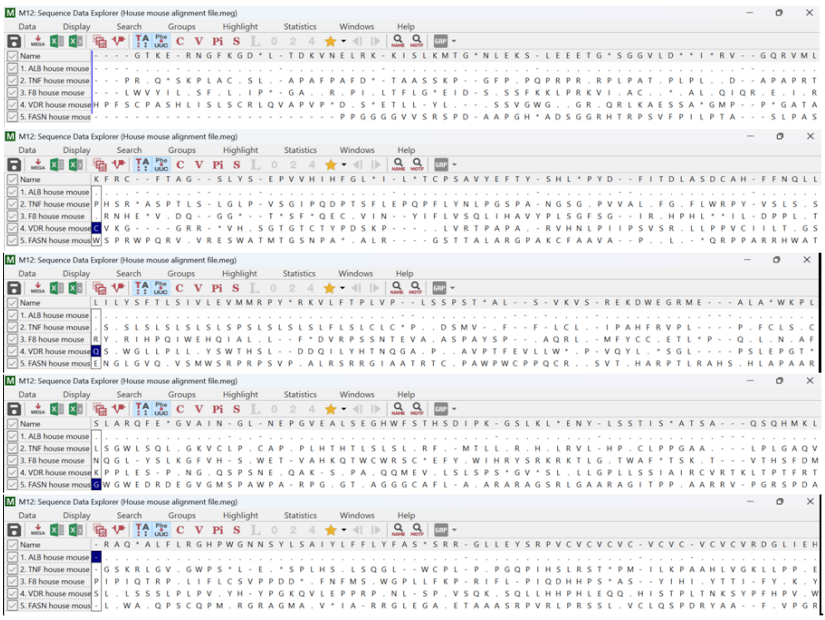

Figure 4D. Translated protein sequences of selected genes in the house mouse, as displayed by ExPASy Translate, showing the resulting amino acid chains.

Figure 4E. Translated protein sequences of selected dog genes, as displayed by ExPASy Translate, showing the resulting amino acid chains.

3.4. Phylogenetic Tree Construction

Phylogenetic trees based on nucleotide and protein sequences were constructed using MEGA 12 with the Tamura-Nei model and the maximum likelihood method. The patterns of clustering mentioned were found: Cow, dog and human genes repeatedly clustered together into a small clade and mouse genes clustered into a distinct, but related branch, diverging to some extent. Chicken genes for all the gene trees were individually clustered apart as the most divergent group. Specific gene clusters surprisingly revealed possible functional associations: TNF and VDR and ALB and FASN, which were often clustered together, suggesting possible functional association or common regulatory networks (Figure 5).

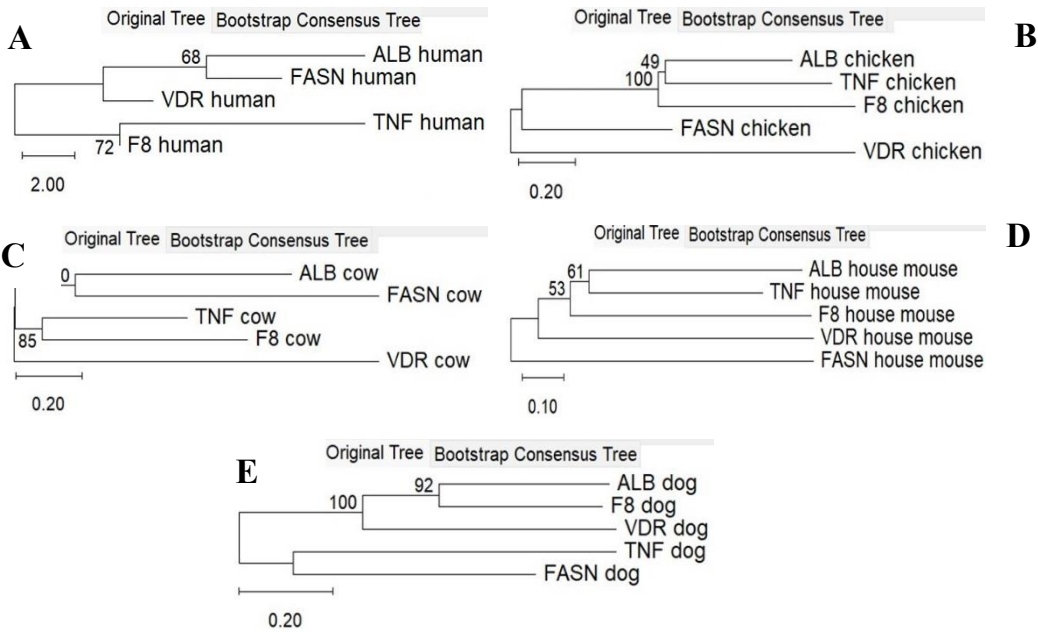

Figure 5. Evolutionary relationships among ALB, TNF, F8, VDR, with A): FASN genes in human, B): FASN genes in chicken, C): FASN genes in cow, D): FASN genes in house mouse and E): FASN genes in dog.

3.5. Protein Structure Modeling

Protein structures were retrieved and presented alongside PDB models. The protein core folds were maintained across species: α-helical segments responsible for transport functions were preserved by ALB proteins. Trimeric structures of TNF proteins with conserved receptor-binding sites were preserved. The conserved A1, A2 and C domains required for clotting function were observed in F8. VDR's typical DNA-binding and ligand-binding domains were preserved. FASN proteins disclosed the multi-domain organization necessary for fatty acid synthesis. The VDR and TNF proteins, particularly in chicken, showed differences in their surface loops, with conserved core domains that may be responsible for their species-specific activity (Figures 6, 7, 8 and 9).

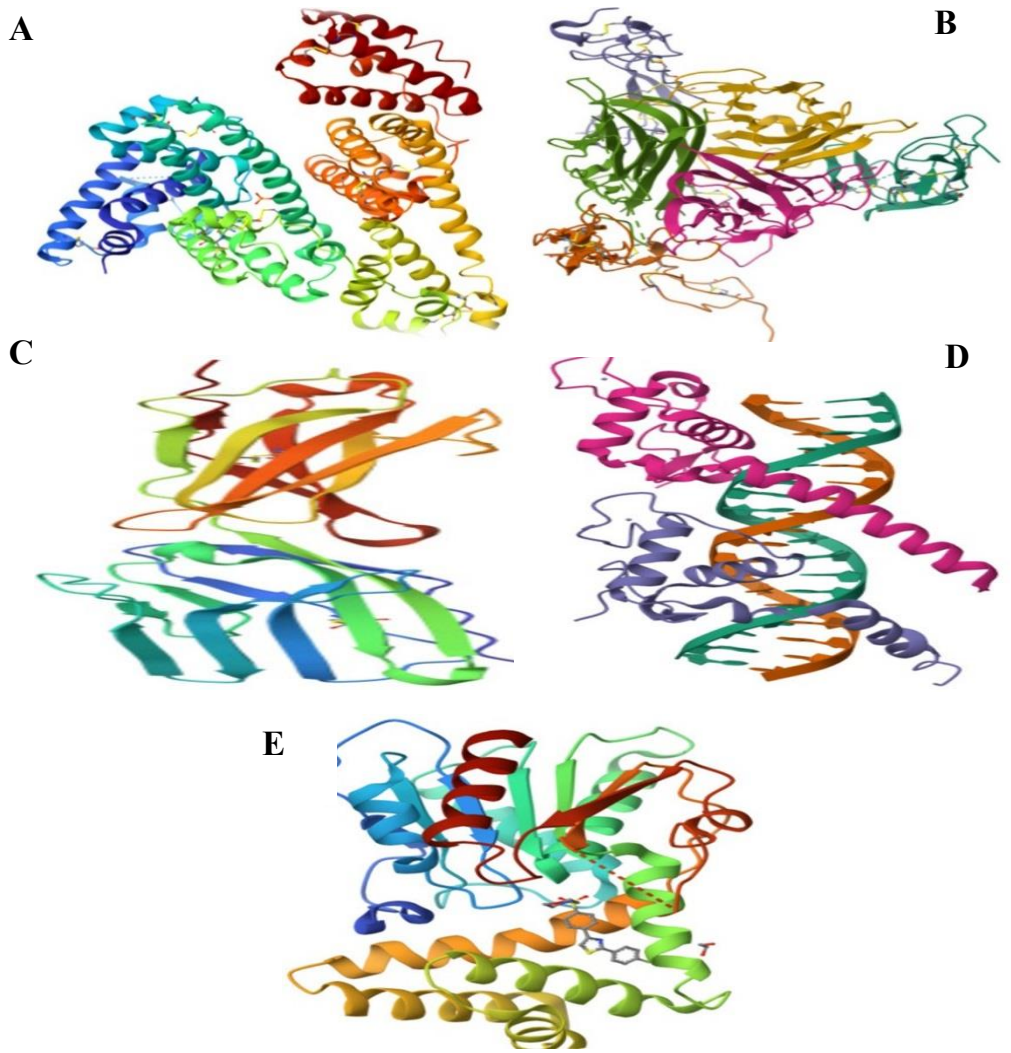

Figure 6. A): Retrieved 3D structure of human ALB (albumin) protein obtained from the PDB database (PDB ID: 1E78) showing its characteristic α-helical domains involved in ligand transport. B): Retrieved 3D structure of human TNF (tumor necrosis factor) protein obtained from the PDB database (PDB ID: 1TNF), showing its trimeric form and conserved receptor-binding interface involved in inflammatory signaling. C): Retrieved 3D structure of human F8 (coagulation factor VIII) protein obtained from the PDB database (PDB ID: 1D7P), showing its domain organization essential for blood coagulation and interaction with von Willebrand factor. D): Ribbon representation of the x-ray monomer compared to predicted 3D structure of human VDR (vitamin D receptor) gene obtained from PDB database (PDB ID: 3A78) representing the ligand binding domain responsible for interaction with vitamin D and regulation of gene transcription. E): The downloaded 3D structure of human FASN protein from PDB (Fatty Acid Synthase); the complex trans-acyltransferase murine fatty acid synthases with substrates gives an overview on how a multi-domain enzyme generates long-chain fatty acids.

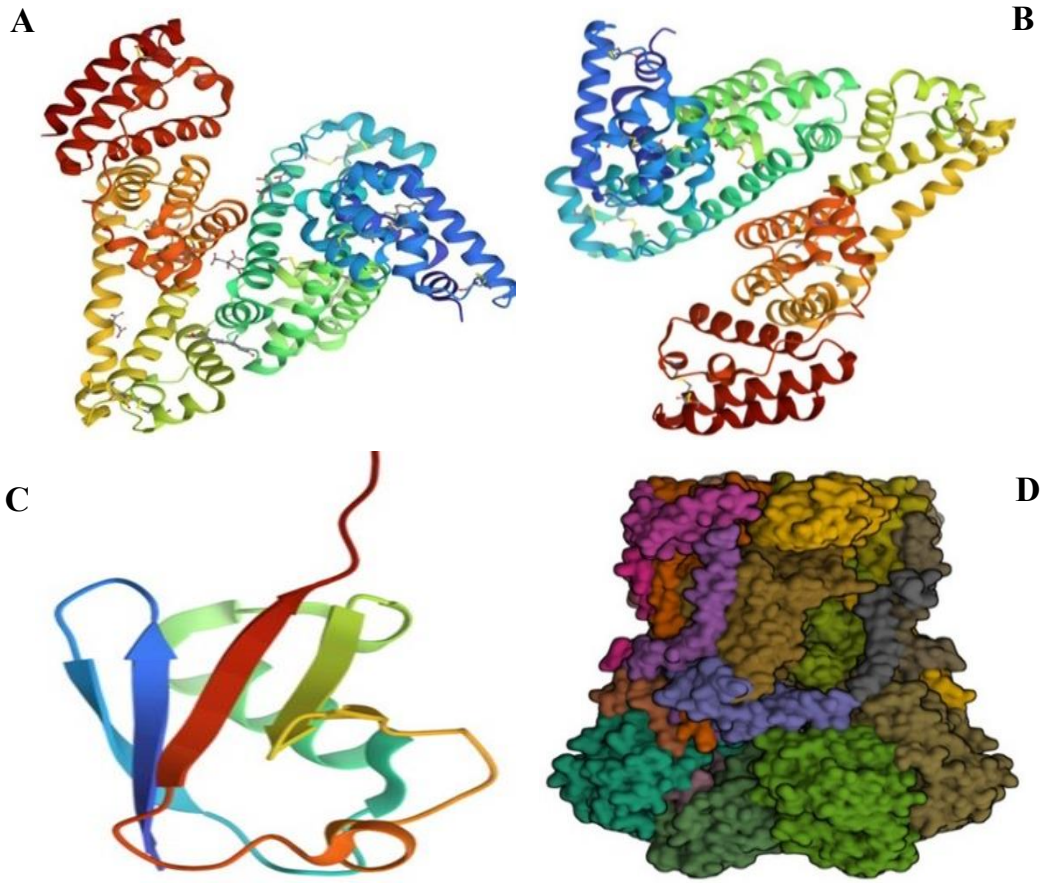

Figure 7. A): Structure of chicken (ALB) protein along with corresponding retrieved from PDB database (PDB ID: AF-P01012-F1); showing conserved α-helical domains participating in ligand transport, analogous to its mammalian orthologs. B): The recovered 3D structure of cow ALB protein (PDB ID: 3V03) from PDB database with recognized conserved α-helical domains typical for serum albumins and are partaking in the transport of fatty acids and other ligands. C): Homology model of cow TNF (tumor necrosis factor) protein using the 3D structure of human TNF from PDB database as template showing trimeric cytokine structural motif and conserved receptor-binding sites implicated in immune signaling. D): PDB-derived structure of cow F8 (coagulation factor VIII) protein illustrating domain architecture required for coagulation and interaction with von Willebrand factor.

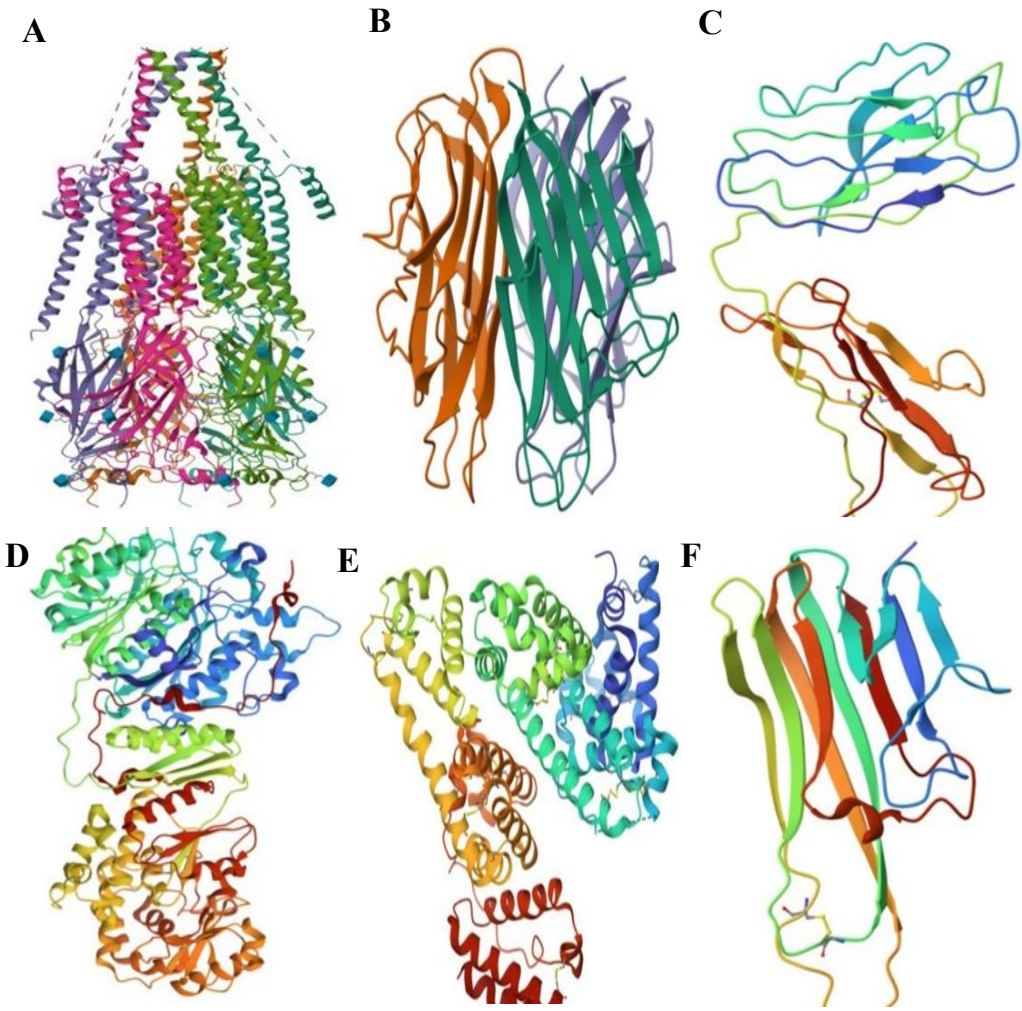

Figure 8. A): Tailored-made image showing the structure of mouse ALB (albumin) protein, as downloaded from PDB. The conserved brown α-helix domains are the regions where ligands bind to and transport substrates. B): Reference 3D structure of mouse TNF (tumor necrosis factor) protein extracted from the PDB database (PDB ID: 2TNF); it is shown in its trimeric cytokine form and has a conserved receptor-binding interface, which directly participates in the immune response. C): Three-dimensional structure of mouse F8 (coagulation factor VIII) protein retrieved from the PDB database (PDB ID: 7K66), demonstrating domain organization important for blood coagulation and interaction with von Willebrand factor. D: The 3D structure of murine FASN (fatty acid synthase) protein retrieved from PDB database (PDB ID: 5MY0), the diagram shows its multi-domain orchestration involved in fatty acid synthesis. E) Extracted 3D structure of dog ALB (albumin) protein from PDB database (ID: 5GHK), with conserved α-helical regions involved in the binding and transport of fatty acids and other ligands depicted. F) Model of the 3D structure of dog TNF (tumor necrosis factor) protein (accession of recovered PDB, 8KB6), revealing its characteristic trimeric cytokine molecule and conserved receptor-interacting surface required for immune signaling.

4. Discussion

The results of the current study confirm that ALB, TNF, F8, VDR and also FASN are liver-

related genes with conserved gene structure and evolutionary patterns in vertebrates as a result of their critical functions in physiology (Spinella & Sahney et al., 2015). Phylogenic clustering pattern of human, dog and cattle sequences was consistent with their expected evolutionary relationships among mammals but not for the avian sequences showing lineage divergence in accordance with vertebrate classification (Alamri et al., 2018; Metcalf et al., 2003; Li et al., 2017). Of the genes examined, ALB and FASN exhibited most consistent transgenomic homology in nucleotide and protein. This is most likely the result of strong evolutionary constraint for these proteins, which play a central role in plasma homeostasis and lipid metabolism (Spinella & Sahney, 2015; Casado & Vallet, 1999; Chirala & Wakil, 2004). Albumin is the major transport protein in vertebrate plasma and its stability has been maintained during evolution (Peters, 1996). Likewise, FASN is essential in the de novo synthesis of fatty acids, a key metabolic function that is necessary for membrane maintenance and energy storage (Menendez et al., 2006; Chirala & Wakil, 2004). The two TNF and F8 were, however, more divergent although for avian sequences in particular. This finding is in line with recent reports that immune signaling molecules evolve under adaptive pressures of exposure to the environment, but also host-pathogen interactions (Aggarwal et al., 2012; Buchmann et al., 2023). Thus, the modest level of variation observed in TNF might reflect functional plasticity within inflammatory pathways, combined with conserved receptor-binding domains critical to biological function (Schwartz et al., 2020).

Likewise, variation in VDR could differentiate species-specific variations in metabolic control. Apart from the classical presentation of VDR involved in calcium homeostasis, activity of VDR has also been reported in hepatic lipid metabolism and modulation of inflammation (Bozic & Guzman, 2016; Ding et al., 2013). Conserved structure of ligand-binding domains and divergence of the regulatory regions imply adaptive fine-tuning rather than functional loss in different species. From a translational standpoint, the F8 retention across mammals is significant due to this gene's importance in blood coagulation, as well as its implication in hemophilia A etiology and therapy (Gitschier et al., 1984; Peyvandi et al., 2016; Wu et al., 2021). Cross-species homology has enabled the use of animal's models to study these coagulopathies and develop gene therapies. Interestingly, there was a clustering pattern indicating potential connections between TNF and VDR because they are involved in regulatory signaling pathways. Cross talk between inflammatory and vitamin D signaling systems has also been reported to modulate immune responses and metabolic homeostasis (Pludowski et al., 2019; Schwartz et al., 2020). In contrast to this and although they share nutritional roles, ALB and FASN seem evolving under different functional constraints. Collectively, the observed strong conservation of metabolic genes in contrast to moderate divergence of immune and signaling genes is consistent with models where housekeeping genes evolve slower than regulatory networks (Krylov et al., 2003). These results support the idea that the core of hepatic metabolic function is structurally conserved among vertebrates, but regulatory elements display evolutionary flexibility. Together, this comparative study emphasizes the tension of evolutionary stability versus functional divergence in liver-related genes and their implications for both evolutionary biology and translational research as well as interspecies disease modeling.

5. Conclusion

Herein we provide a comparative evolutionary view of five major liver-involved genes (ALB, TNF, F8, VDR and FASN) across vertebrate species. The results indicate that the core metabolic genes, especially ALB and FASN had more conservation because of their crucial impact on body physiology homeostasis. However, genes with adaptive flexibility in the context of species-specific environments and physiology such as TNF and VDR, related to regulation/immune system development, with a moderate level of divergence. Structural motifs are conserved in a variety of species, indicating that important biological functions remain stable over evolution. Such an observation is consistent with the more general finding that metabolic housekeeping genes are highly constrained and signaling pathways retain adaptive variance. In conclusion, the integrative bioinformatics approach in this study emphasizes the evolutionary conservation of

hepatic functional networks and the importance of comparative genomics in interpreting liver biology, translational disease models and cross-species functional conservation.

Author Contributions

Mamoona Mushtaq, Muhammad Asif Shabbir, Fizza Shahid, Ayesha Sattar, and Naureen Anwar contributed to the conceptualization, research design, methodology, selection of liver-associated genes and vertebrate species, retrieval and curation of nucleotide and protein sequences, multiple-sequence alignment, phylogenetic analysis, conserved-domain identification, protein-structure comparison, interpretation of findings, and preparation of the manuscript. All authors contributed to writing—original draft and writing—review and editing. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that they have no financial, professional, institutional, commercial, or personal conflicts of interest that could have influenced the conduct, analysis, interpretation, or reporting of this study.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability

The nucleotide and protein sequences analysed in this study were obtained from publicly available databases, including the National Center for Biotechnology Information and the Protein Data Bank. The accession numbers of the analysed sequences are provided in the manuscript. Additional sequence alignments, phylogenetic files, conserved-domain results, and analytical outputs may be obtained from the corresponding author upon reasonable request.

Informed Consent

Not applicable. The study did not involve direct participation by human subjects or the use of identifiable personal or clinical information.

Use of Generative AI

The authors declare that no generative artificial intelligence tools were used to retrieve or analyse the sequence data, perform the phylogenetic and conserved-domain analyses, generate the scientific content, interpret the findings, or formulate the conclusions presented in this article.

6. References

Aggarwal, B. B., Gupta, S. C., & Kim, J. H. (2012). Historical perspectives on tumor necrosis factor and its superfamily: 25 years later. *Blood*, *119*(3), 651–665. https://doi.org/10.1182/blood-2011-04-325225

Alamri, A., Alshahrani, M., & Alqahtani, A. (2018). Liver physiology and metabolism. *International Journal of Biological Sciences*, *14*(5), 499–512. https://doi.org/10.7150/ijbs.24374

Barton, G. M., Sacks, D. B., & Janeway, C. A. (1990). Tumor necrosis factor and autoimmune disease. *Immunology Today*, *11*(5), 165–168. https://doi.org/10.1016/0167-5699(90)90037-S

Bashir, I., Shabbir, M. A., Shahid, F., Sattar, A., & Anwar, N. (2025). Phylogenetic analysis of cancerous genes (human) for conserved domains using bioinformatics tool. *Medical and Life Sciences*, 4(2), 01–12.

Bozic, M., & Guzman, C. (2016). Vitamin D receptor expression in liver and its role in metabolic homeostasis. *Journal of Hepatology*, *64*(6), 1350–1357. https://doi.org/10.1016/j.jhep.2016.02.002

Buchmann, G., Müller, C., Hernández-Rodríguez, D., et al. (2023). Vertebrate TNF superfamily: Evolution and functional insights. *Biology*, *12*(3), 405. https://doi.org/10.3390/biology12030405

Casado, M., & Vallet, V. (1999). Fatty acid synthase and its relevance in metabolic regulation. *Biochemical Journal*, *343*, 505–512. httpsd://doi.org/10.1042/bj3430505

Cavusoglu, E., Sari, U., & Tiryaki, I. (2023). Genome-wide identification and expression analysis

of Na+/H+ antiporter (NHX) genes in tomato under salt stress. *Plant Direct*, *7*(11), e543. https://doi.org/10.1002/pld3.543

Chirala, S. S., & Wakil, S. J. (2004). Structure and function of animal fatty acid synthase. *Lipids*, *39*(11), 1045–1053. https://doi.org/10.1007/s11745-004-1339-9

Ding, N., Yu, R. T., Subramaniam, N., et al. (2013). A vitamin D receptor/SMAD genomic circuit gates hepatic fibrotic response. *Cell*, *153*(3), 601–613. https://doi.org/10.1016/j.cell.2013.03.028

Gitschier, J., Wood, W. I., Goralka, T. M., Wion, K. L., Chen, E. Y., Eaton, D. H., Vehar, G. A., Capon, D. J., & Lawn, R. M. (1984). Characterization of the factor VIII gene in hemophilia A. *Nature*, *312*, 326–330. https://doi.org/10.1038/312326a0

Green, D. (2024). Hemophilia and Other Congenital Coagulopathies in Women. *Journal of Hematology*, *13*(4), 137.

Kabiraj, A., Laha, A., Panja, A. S., & Bandopadhyay, R. (2023). In silico comparative structural and functional analysis of arsenite methyltransferase from bacteria, fungi, fishes, birds, and mammals. *Journal of Genetic Engineering and Biotechnology*, *21*(1), 64. https://doi.org/10.1186/s43141-023-00522-9

Krylov, D. M., Wolf, Y. I., Rogozin, I. B., & Koonin, E. V. (2003). Gene loss, protein sequence divergence, gene dispensability, expression level and interactivity are correlated in eukaryotic evolution. *Genome Research*, *13*(10), 2229–2235. https://doi.org/10.1101/gr.1589103

Li, S., Cao, Y., Geng, F., et al. (2017). Genome-wide identification and comparative analysis of albumin family in vertebrates. Evolutionary *Bioinformatics*, *13*, 1–9. https://doi.org/10.1177/1176934317728915

Menendez, J. A., Vellon, L., Mehmi, I., Oza, B. P., Ropero, S., & Lupu, R. (2006). Fatty acid synthase: Association with metabolic disease and cancer. *Clinical Cancer Research*, *12*(18), 5399–5403. https://doi.org/10.1158/1078-0432.CCR-06-0453

Metcalf, V., Brennan, S., George, P., et al. (2003). Using serum albumin to infer vertebrate phylogenies. *Applied Bioinformatics*, *2*(3), 135–141.

Mohajan, H. K. (2025). A study on functions of liver to sustain a healthy liver. *Innov Sci Technol*, *4*(1), 77–87.

Nie, S., Huang, P., Niu, H., Ding, F., Gong, L., Zou, C., ... & Yang, G. (2025). Vitamin D deficiency enhances platelet activation and thrombosis by regulating VDR/Akt pathway based on platelet proteomics. *European Journal of Pharmacology*, *999*, 177684. https://doi.org/10.1016/j.ejphar.2025.177684

Peters, T. (1996). *All about albumin: Biochemistry, genetics and medical applications*. Academic Press.

Peyvandi, F., Garagiola, I., & Young, G. (2016). The past and future of haemophilia: Diagnosis, treatments and its complications. *The Lancet*, *388*(10040), 187–197. https://doi.org/10.1016/S0140-6736(15)01123-X

Pludowski, P., Holick, M. F., et al. (2019). Vitamin D in disease prevention and treatment: A review. *Nutrients*, *11*(3), 646. https://doi.org/10.3390/nu11030646

Ramagopalan, S. V., Maugeri, N. J., Handunnetthi, L., Lincoln, M. R., Orton, S. M., Dyment, D. A., Herrera, B. M., DeLuca, G. C., & Ebers, G. C. (1999). VDR gene polymorphisms and susceptibility to autoimmune diseases. *Immunogenetics*, 50, 301–309. https://doi.org/10.1007/s002510050593

Schwartz, D. M., Kanno, Y., Villarino, A. V., Ward, M., Gadina, M., & O'Shea, J. J. (2020). Targeting TNF signaling in inflammation and disease. *New England Journal of Medicine*, *382*, 1293–1303. https://doi.org/10.1056/NEJMra1906351

Singh, S., Karthikeyan, C., & Moorthy, N. S. H. N. (2024). Fatty acid synthase (FASN): A patent review since 2016-present. *Recent Patents on Anti-Cancer Drug Discovery*, *19*(1), 37-56. https://doi.org/10.2174/1574892818666230112170003

Spinella, R. C., & Sahney, S. (2015). Albumin: Physiological function and role in clinical diagnosis. Clinical Biochemistry, 48, 314–319. https://doi.org/10.1016/j.clinbiochem.2014.12.001

Trefts, E., & Gannon, M. (2017). The liver: A regulator of metabolism. *Nature Reviews Endocrinology*, *13*(5), 233–244. https://doi.org/10.1038/nrendo.2017.8

Vandepoele, K., Thierens, S., & Van Bel, M. (2024). Northern light reviews–Application of orthology and network biology to infer gene functions in non-model plants. *Physiologia Plantarum*, *176*(4), e14441. https://doi.org/10.1111/ppl.14441

Wang, H., Yan, Z., Yang, M., & Gu, L. (2023). Genome-wide identification and characterization of the diacylglycerol kinase (DGK) gene family in Populus trichocarpa. *Physiological and Molecular Plant Pathology*, *127*, 102121. https://doi.org/10.1016/j.pmpp.2023.102121

Wu, X., Gao, Y., Zhang, L., & Wang, Y. (2021). Gene editing for hemophilia A: CRISPR-mediated correction of F8 mutations. *Nature Communications*, *12*, 2414. https://doi.org/10.1038/s41467-021-22662-2

Yosilia, R., Afandi, A., Hoya, A. L., Cahyani, C. N., & Hieno, A. (2024). Phytophthora palmivora Relationship Analysis on ITS rDNA Primers Using MEGA11 Software (NCBI DNA Sequencing Library Study). *Jurnal Agrotek Tropika*, *12*(4), 1020–1031. https://doi.org/10.23960/jat.v12i4.9532

Zhang, C., Zhang, Y., Liu, B., Chen, Y., Xie, Y., Huang, H., ... & He, Z. (2024). Proteome and metabolome profiling of anticoagulant disorders induced by familial protein S deficiency. *Journal of Proteome Research*, *23*(10), 4538–4552.