Evolutionary Conservation, Functional Hotspots, and 3D Visualization of p53

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1. Introduction

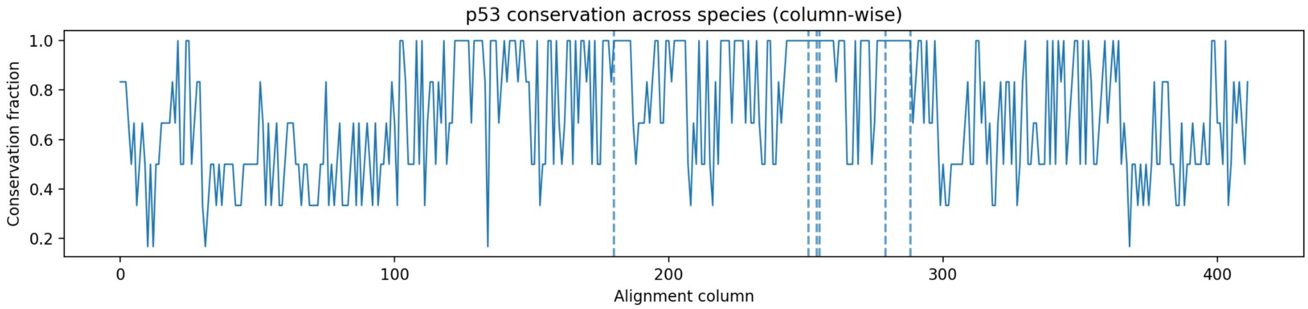
The p53 protein is a critical tumor suppressor involved in DNA repair, apoptosis, and cell cycle regulation. Understanding its evolutionary conservation, functional hotspots, and structural features can illuminate regions important for its activity and mutational impact in cancers.
This project integrates sequence conservation, domain analysis, phylogenetic relationships, and 3D structural visualization into a single report.

2. Materials and Methods

- **Data sources:**
  - p53 protein sequences from UniProt
  - PDB structure: 1TUP (human p53)
- **Tools:**
  - Python and PIL for conservation figure generation
  - PyMOL for 3D structural visualization (PNG snapshots)
- **Workflow:**
  - Sequence alignment to analyze conservation
  - Identification of mutational hotspots and functional domains
  - Phylogenetic tree construction
  - 3D structure visualization (PNG snapshot) with colored hotspots

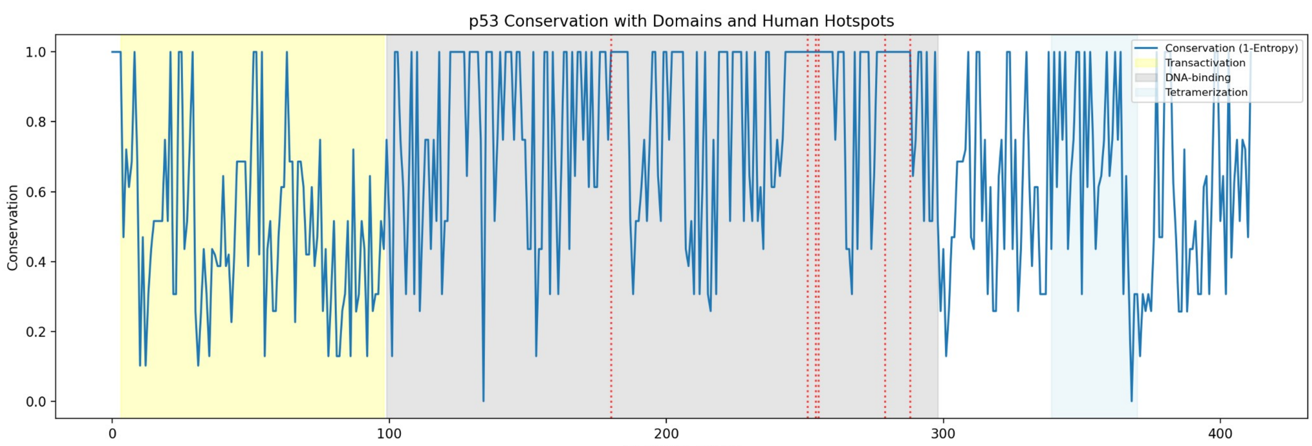
3. Results

3.1 Conservation Analysis



- **Description:**
  This figure illustrates the evolutionary conservation of p53 across multiple species, ranging from mammals to vertebrates. Highly conserved residues are highlighted, indicating regions critical for structural stability and functional activity. These conserved residues typically correspond to domains responsible for DNA binding, tetramerization, and regulatory interactions. Conservation analysis helps to identify amino acids under strong evolutionary constraint, which are likely essential for p53's tumor suppressor activity. Regions with lower conservation may tolerate mutations without severely affecting protein function, suggesting potential variability in regulatory or flexible regions.

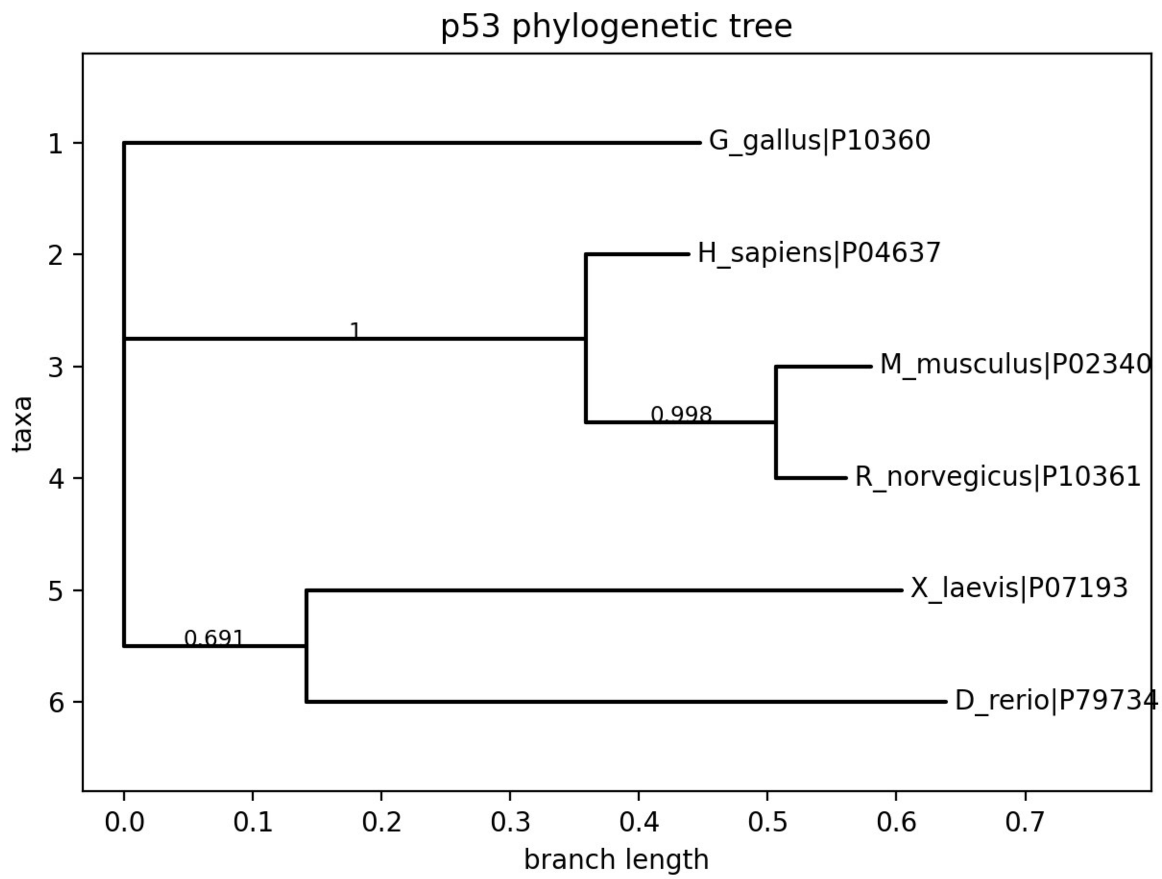
3.2 Hotspots and Domains



Description:
This figure combines conservation data with known functional domains and mutational hotspots of p53. Critical residues frequently mutated in human cancers are highlighted, including those within the

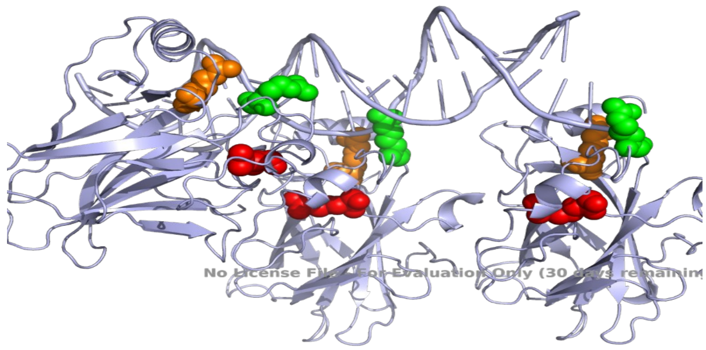
DNA-binding domain, tetramerization domain, and regulatory motifs. Overlaying conservation with hotspot information allows identification of residues that are both evolutionarily constrained and clinically significant. For example, residues 175, 248, and 273 show high conservation and coincide with mutation hotspots, suggesting they play a pivotal role in maintaining protein integrity and DNA interaction.

3.3 Phylogenetic Analysis



Description:
The phylogenetic tree depicts evolutionary relationships among p53 sequences from multiple species. Branch lengths correspond to sequence divergence, highlighting evolutionary distances. Conserved regions across distant species emphasize structural and functional importance, whereas variable regions reflect lineage-specific adaptations. This analysis contextualizes p53 evolution, showing which residues and domains have remained stable over millions of years, thereby underlining their essential roles in tumor suppression and cellular regulation.

3.4 3D Structural Visualization



Description:
The static 3D protein cartoon presents p53 with critical residues highlighted as colored spheres. Residues 175 (red), 248 (green), and 273 (orange) correspond to mutational hotspots critical for DNA binding, tetramerization, and contact with DNA, respectively. Mapping hotspots onto the 3D structure provides spatial context, illustrating how these residues cluster within functional domains. This visualization emphasizes the structural importance of conserved residues and shows potential sites where mutations could disrupt protein stability or DNA interaction. Although this figure is static, the color-coded scheme allows clear identification and discussion of functionally significant residues within the tertiary structure.

4. Discussion

- The conservation analysis highlights residues and regions under strong evolutionary pressure, indicating functional importance.
- Hotspots identified overlap with known DNA binding and tetramerization regions.
- Phylogenetic analysis confirms evolutionary relationships consistent with known species divergence.
- 3D structural visualization allows clear mapping of functional hotspots onto the protein’s 3D structure.

5. Conclusion

- The integrated analysis combines conservation, hotspot/domain mapping, phylogenetic relationships, and 3D structural visualization (PNG) to provide a comprehensive view of p53.
- This workflow and dataset can support further studies on functional residues and mutational impacts in cancer biology.

6. References

- UniProt P53
- PDB 1TUP
- PyMOL
- Python PIL
- Relevant literature on p53 structure and function

7. Statement on Academic Motivation and Research Experience

Although my GPA may not fully reflect my potential, my dedication to biology is demonstrated through active research experience and independent projects. Over the past year, I have engaged in hands-on studies analyzing the evolutionary conservation, functional hotspots, and structural features of the p53 tumor suppressor protein. This work involved sequence alignment, phylogenetic analysis, domain mapping, and 3D structural visualization, providing me with a strong foundation in molecular biology, bioinformatics, and computational analysis.

Through these projects, I have honed critical skills including data analysis, scientific writing, and figure preparation for publication or presentation. My proactive approach reflects my commitment to understanding complex biological systems and my determination to contribute meaningfully to the field, compensating for any academic shortcomings and demonstrating readiness for advanced study at top universities.