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In silico Analysis of a Three-Finger Toxin from *Micrurus corallinus* Suggests Anticoagulant Potential through Structural Homology with *Hemachatus haemachatus* Toxins

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INTRODUCTION

Three-finger toxins (3FTx) are a diverse group of non-enzymatic polypeptides found in snake venoms, named for their common structure consisting of three beta-strand loops connected to a central core containing four or five conserved disulfide bonds. Known for their broad range of biological activities, this study focuses on a specific 3FTx from the venom of the coral snake *Micrurus corallinus* (3FTx1 - Uniprot: C6JUP0_MICCO). The objective is to identify potential biological targets for this toxin using advanced bioinformatics tools

METHOD

The bioinformatics tools used in this study include AlphaFold2, Rosetta docking, and the DALI server. First, AlphaFold2 was employed to model the three-dimensional structure of 3FTx1 with high accuracy. With the modeled structure, Rosetta docking was used to evaluate the toxin's potential interactions with three specific receptors: the nicotinic acetylcholine receptor (nAChR), the muscarinic M1 acetylcholine receptor (M1_mAChR), and the alpha-7 nicotinic acetylcholine receptor (α7_nAChR). Finally, the DALI server was applied to compare the toxin's structure with known proteins, identifying potential functional homologs.

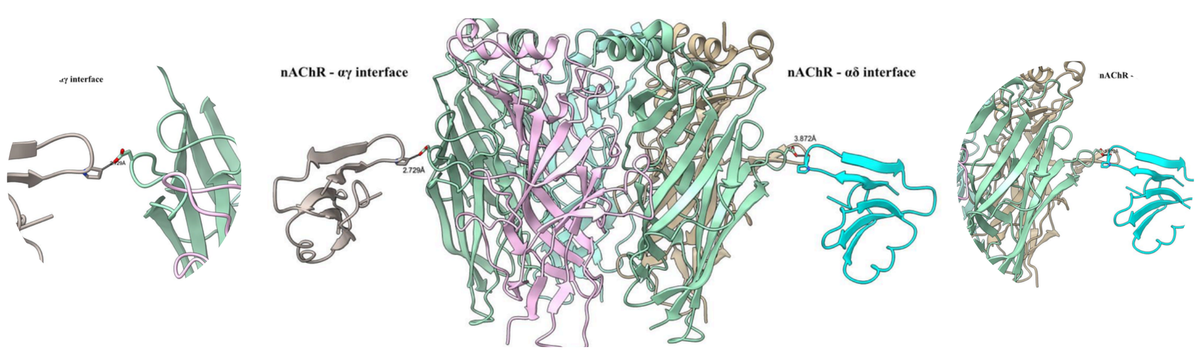

Image 1 - Nicotinic acetylcholine receptor with 3FTx1, showing no efficient binding in docking analysis.

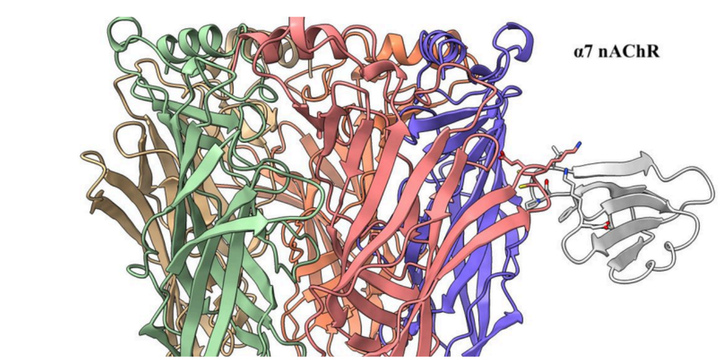

Image 2 - Showing that 3FTx1 also failed to bind to the α7 nicotinic neuronal receptor.

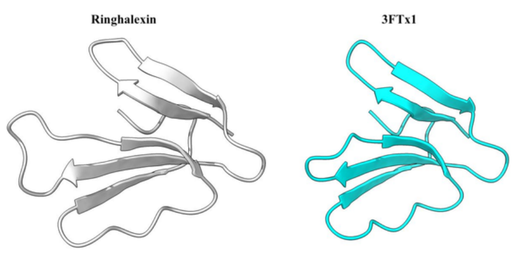

Image 3 - Side-by-side comparison of 3FTx1 and Ringhalexin.

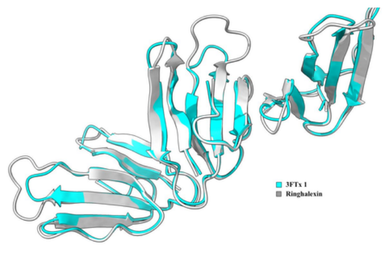

Image 4 - Alignment of 3FTx1 with Ringhalexin.

RESULTS & DISCUSSION

After modelling its structure using AlphaFold, Rosetta docking results with the highest-quality structure indicated that 3FTx1 does not establish significant interactions with nAChR, M1_mAChR, or α7_nAChR, which are common targets for this class of toxins. Protein structure comparison using DALI revealed that 3FTx1 shares significant similarity with toxins from *Hemachatus haemachatus*, specifically Ringhalexin (Uniprot: 3SO1_HEMHA) and a cytotoxin homologue (Uniprot: 3SOE_HEMHA). Ringhalexin is known to act as a potent inhibitor of Factor X activation by the extrinsic tenase complex and as a weak, irreversible neurotoxin, highlighting its dual functionality and suggesting a potential shared functional role between these toxins.

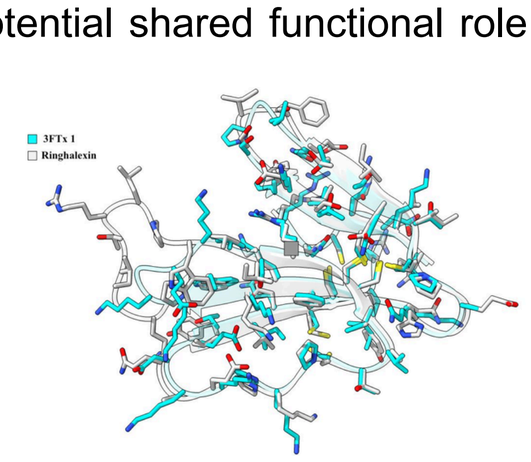

Image 5 - Side chain alignment of 3FTx1 with Ringhalexin.

CONCLUSION

The *Micrurus corallinus* 3FTx1 exhibits structural similarities to toxins with known anticoagulant properties rather than neurotoxic effects. This suggests a potential anticoagulant action for this toxin, which aligns with the functional characteristics of its structural homologs from *Hemachatus haemachatus*. Further experimental studies are required to validate these findings and elucidate the exact biological activities of this 3FTx.

FUTURE WORK / REFERENCES

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