IECBS IECNS 2026 Conference

The 5th Intl Electronic Conference on Brain Sciences & 1st Intl Electronic Conference on Neurosciences

9–11 March 2026 | Online

MDPI

Computational Modeling and Molecular Dynamics of Nonsynonymous *CSDE1* Variants Associated with Autism Spectrum Disorder

Mehwish Majeed[1,2], Muhammad Zurgham Akram[1,2]

[1]College of Medicine and Biological Information Engineering, Northeastern University, Shenyang, Liaoning, 110819, China.

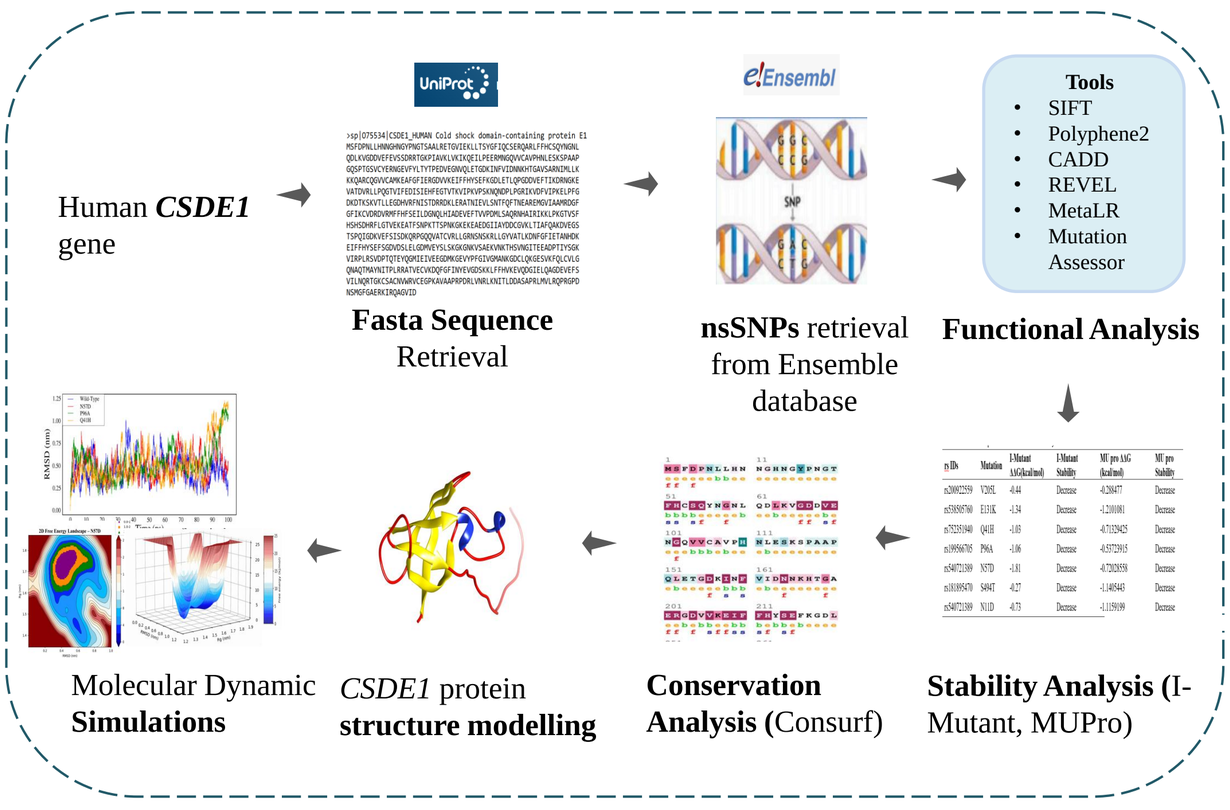
[2]Department of Computer Science, University of Agriculture Faisalabad, Agriculture University Road, 38000, Faisalabad, Pakistan.

INTRODUCTION & AIM

Autism Spectrum Disorder (ASD) is a complex genetic neurodevelopmental disorder. A post-transcriptional regulator, *CSDE1*, has been identified as a candidate susceptibility gene in ASD, but the structural and functional impact of its coding variants remains largely unexplored.

This study aimed to systematically characterize the structural and dynamic effects of nonsynonymous single-nucleotide polymorphisms (nsSNPs) in *CSDE1* associated with Autism Spectrum Disorder using an integrative computational framework.

METHOD



RESULTS & DISCUSSION

Variant Prioritization

Seven deleterious nsSNPs identified from which three variants including **Q41H, N57D,** and **P96A** were selected for molecular dynamic simulations based on combined evidence of pathogenicity scores, perturbation stability, and evolutionary conservation

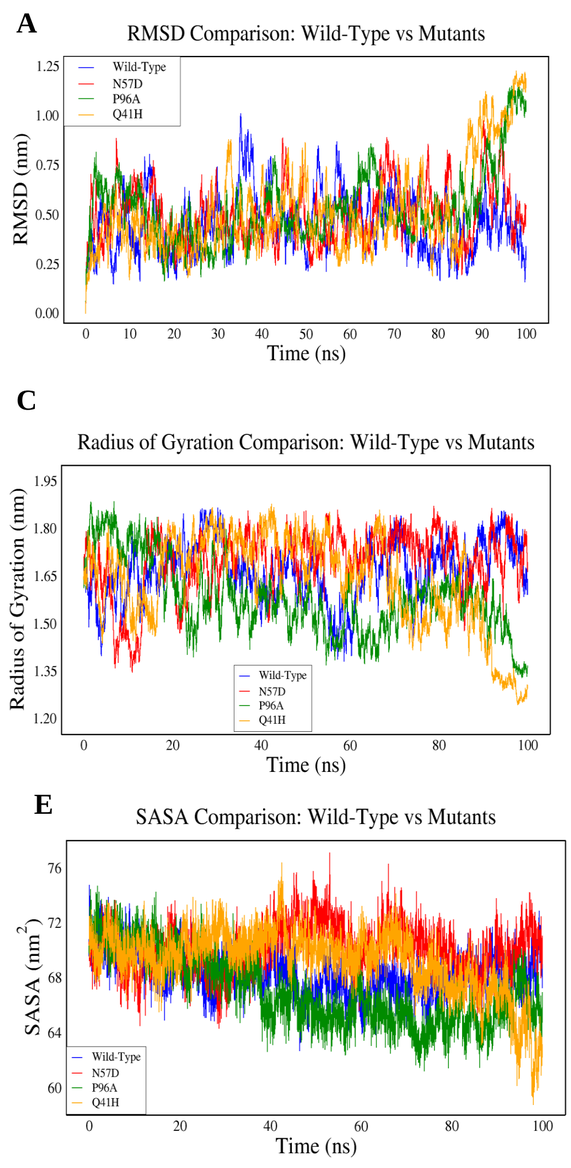
Table 1. Stability Analysis of nsSNPs on *CSDE1*

rs IDs	Mutation	I-Mutant ΔΔG(kcal/mol)	I-Mutant Stability	MU pro ΔΔG (kcal/mol)	MU pro Stability
rs200922559	V205L	-0.44	Decrease	-0.288477	Decrease
rs538505760	E131K	-1.34	Decrease	-1.2101081	Decrease
rs752351940	Q41H	-1.03	Decrease	-0.71329425	Decrease
rs199566705	P96A	-1.06	Decrease	-0.53723915	Decrease
rs540721389	N57D	-1.81	Decrease	-0.72028558	Decrease
rs181895470	S494T	-0.27	Decrease	-1.1405443	Decrease
rs540721389	N11D	-0.73	Decrease	-1.1159199	Decrease

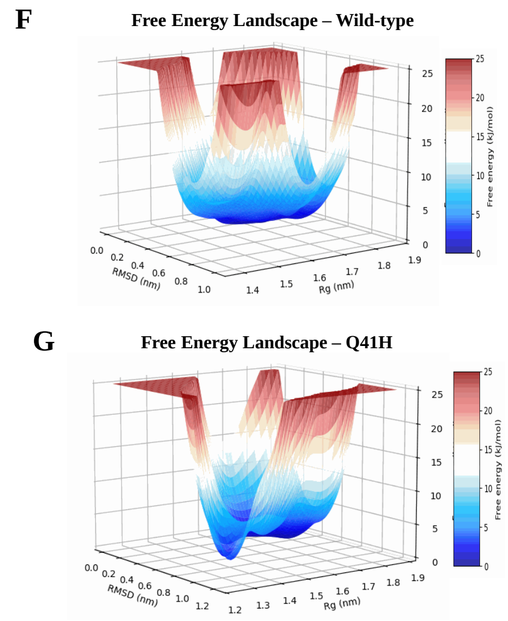
Evolutionary Conservation

Q41H mutations were classified as highly conserved, P96A variant showed intermediate conservation and N57D were categorized as variable conservation.

Molecular dynamic simulations and Free energy landscape



From MD simulations and FEL analysis Q41H emerged as most destabilizing variant exhibited highest RMSD, increased flexibility, reduced hydrogen bonding, increased solvent exposure, broad, shallow FEL basin.



Whereas, N57D showed structural expansion and moderate conformational dispersion. Lastly, P96A maintained near-native hydrogen bonding, narrow energy basin similar to wild type.

These mutation-driven dynamic alterations suggest a potential mechanistic link between *CSDE1* structural perturbation and ASD pathogenesis.

CONCLUSION

This integrative computational investigation identifies Q41H as the most structurally disruptive *CSDE1* variant, markedly altering stability and conformational behavior. These mutation-driven structural perturbations provide a potential mechanistic link between *CSDE1* dysfunction and ASD pathogenesis.

FUTURE WORK / REFERENCES

Future work should focus on experimental validation of Q41H to confirm its role in *CSDE1* dysfunction and ASD pathogenesis.

Zhuang H, Liang Z, Ma G, et al. Autism spectrum disorder: pathogenesis, biomarker, and intervention therapy. *MedComm*. 2024;5(3). doi:https://doi.org/10.1002/mco2.497

Guo H, Li Y, Shen L, et al. Disruptive variants of CSDE1 associate with autism and interfere with neuronal development and synaptic transmission. Science Advances. 2019;5(9). doi:https://doi.org/10.1126/sciadv.aax2166