

A SIMULATION STUDY OF THE EFFECT OF NATURALLY OCCURRING POINT MUTATIONS ON THE SRY-DNA COMPLEX

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ABSTRACT

We present recently published results [1] on investigating the effect of the naturally occurring point mutations of the transcription factor (TF) sex-determining region Y (SRY) on the structure and dynamics of the SRY-DNA complex, by means of μ s-long Molecular dynamics (MD) simulations. TFs are DNA-binding proteins that act as major regulators of gene expression and cellular differentiation. The wild-type SRY along with two mutants, I13T and G40R, comprising point mutations on the SRY chain, which have been clinically identified in patients with sex developmental disorders, were modeled as DNA complexes. The results suggest that the observed disorders brought about by the G40R-DNA and I13T-DNA may arise predominantly from the destabilization of the complex being in accord with *in vitro* assays found elsewhere and from modifications of the DNA bending as revealed in our study. In addition, comparative potential of mean force computations over a sequence of short separation distances for the three complexes, verified a higher stability of the normal SRY-DNA. Ultimately, examining the way the SRY mutations modulate the SRY-DNA complex dynamics at the microscopic level, is important also toward elucidating molecular determinants of function for proteins capable of binding to DNA, which in a broader context may contribute to novel therapeutic routes that target the transcriptome.

KEYWORDS: Transcription Factors, Gene Expression, Mutations, Computer Simulation

REFERENCES

[1] Nasou A. G., Pantatosaki E., Papadopoulos G. K. (2022). J. Phys. Chem. B, 126(44), 8921–8930.