



Abstract

A Molecular Dynamics Simulation Study of the Arg206Cys Variant in DNASE1L3 Enzyme [†]

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[†] Presented at the 2nd International Electronic Conference on Biomolecules: Biomacromolecules and the Modern World Challenges, 1–15 November 2022; Available online: <https://iecbm2022.sciforum.net/>.

Abstract: Genome-wide association studies (GWAS) have identified that one of the autoimmune disease-associated loci, predisposing for the development of Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA) and Systemic Sclerosis (SSc), is the rs35677470 missense variant of the Deoxyribonuclease I like 3 (*DNASE1L3*) gene, leading to R206C substitution in *DNASE1L3* enzyme. Molecular Dynamics (MD) simulations were implemented for the wild type and mutated enzyme, in order to investigate the structure-function relationship that leads to partial loss of enzyme function. Results showed loss of salt bridges, larger fluctuation in active site regions and lower charge of the catalytic and DNA binding sites after the mutation. The present study raises the necessity of in silico methods, in understanding and managing autoimmune diseases.

Keywords: *DNASE1L3*; molecular dynamics simulations; MD; single nucleotide polymorphism; rs35677470; autoimmune diseases; Systemic Lupus Erythematosus (SLE); Rheumatoid Arthritis (RA); Systemic Sclerosis (SSc)



Citation: Skarlatou, M.; Andreou, A.;

Christoforides, E.; Thireou, T. A

Molecular Dynamics Simulation Study of the Arg206Cys Variant in DNASE1L3 Enzyme. *Biol. Life Sci. Forum* **2022**, *20*, 10. <https://doi.org/10.3390/IECBM2022-13378>

Academic Editor: Vladimir Uversky

Published: 1 November 2022

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Supplementary Materials: The following are available online at <https://www.mdpi.com/article/10.3390/IECBM2022-13378/s1>.

Author Contributions: Conceptualization, A.A., and T.T.; visualization, M.S., A.A., E.C.; methodology and validation, formal analysis, investigation, data curation, M.S., A.A., E.C., T.T.; writing—original draft preparation, writing—review and editing, A.A., E.C., T.T.; supervision, T.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Acknowledgments: We acknowledge support of this work by the project “INSPIRED—The National Research Infrastructures on Integrated Structural Biology, Drug Screening Efforts and Drug Target Functional Characterization” (Grant MIS 5002550), which is implemented under the Action “Reinforcement of the Research and Innovation Infrastructure”, funded by the Operational Programme “Competitiveness, Entrepreneurship and Innovation” (NSRF 2014–2020) and co-financed by Greece and the European Union (European Regional Development Fund). Authors are grateful to Elias Eliopoulos for fruitful discussion and assistance throughout all aspects of our study, Kostas Bethanis and George Goulielmos for suggestions and discussion.

Conflicts of Interest: The authors declare no conflict of interest.