

Abstract

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

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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 structural changes and loss of 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)

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