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Missense NEXN-rs1166698 Gene Polymorphism May Correlate to Protein Structural Disruptions in Cardiomyocytes: An *In-Silico* Study

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Abstract

Nexilin, encoded by the *NEXN* gene, is a vital actin-binding protein that plays a crucial role in maintaining the structural integrity of cardiomyocytes [1]. Disruptions in its structure may contribute to cardiac dysfunction [2]. In this in silico study, we focused on the structural impact of the rs1166698 single nucleotide polymorphism (SNP) (G>A, Gly181Arg) within the *NEXN* gene. Using bioinformatics tools such as SIFT, PolyPhen-2, and Mutation Assessor, we assessed the Gly181Arg substitution and found it deleterious, indicating potential disruption in protein function. Structural stability analysis performed by I-Mutant, iStable, and MUpro predicted a significant reduction in nexilin's stability due to this mutation, suggesting that the protein may lose its ability to maintain proper mechanical support in heart cells. Furthermore, secondary structure predictions from PSIPRED and GOR-IV showed that the Gly181Arg substitution may alter the folding pattern of nexilin, affecting its structural conformation and potentially leading to functional impairments. As nexilin plays a critical role in anchoring actin filaments, these structural alterations could disrupt the cytoskeletal organization in cardiomyocytes, contributing to arrhythmogenic conditions [3]. Therefore, this study identifies the rs1166698 polymorphism as a potentially significant factor in nexilin dysfunction, warranting further investigation into its role in protein structure and arrhythmia development.

Key words: Missense SNP, *NEXN* gene, protein stability, protein structure, rs1166698.

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