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Abstract Topic: - Clinical Genetics

Abstract Title: - The implication of ENSA,ABCC8,KCNJ11 gene variations in Type 1 Diabetes expediting to personalized medicine

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Aims: - Type 1 diabetes mellitus (TIDM), a polygenic disorder, causes hyperglycemia inferable from insulin deficiency and involves various genetic and environmental factors.

The KATP channel is an octameric complex encoded by KCNJ11 and ABCC8 genes. ENSA is an endogenous ligand that mimics the action of sulfonylureas. Sulfonyl ureas inhibit KATP channel opening and thus stimulate insulin release. ENSA inhibits sulfonylurea binding to b-cell membranes, decreases cloned KATP channel currents, and promotes b-cell insulin secretion.

Mutations in the genes ENSA, ABCC8, and KCNJ11 disrupt the potentiality of the KATP channel and regulate the secretion of insulin by detecting a change in the blood glucose level and consequently maintaining glucose homeostasis. The present study was designed to investigate the association of ENSA, ABCC8, and KCNJ11 gene polymorphisms with type 1 diabetes

Methods: - A case-control study was conducted enrolling 100 cases of T1DM and 100 healthy controls of comparable age and sex. Gene variations were determined by PCR-RFLP and ARMS-PCR methods, and molecular docking.

Results: - The ABCC8-3C > T (rs1799854) variation was found to be significantly associated with T1DM ($p<0.01$) and “CT” genotype was found to be predominant in T1DM with a threefold increased risk to diabetes and the association was statistically significant. but we did not observe any significant association of G>A (rs5215) polymorphism of KCNJ11 with T1DM. Further ENSA C>T (rs1053732) variation was found to be significantly associated with T1DM ($p<0.01$).

In the current in silico study, sulfonyl urea drug was docked against SUR receptor using CB-dock. A vina score of -7.6 was obtained and the binding site of the SUR receptor is surrounded by amino acids such as Threonine, Phenylalanine, and Alanine

Conclusions: - The current study emphasizes the significance of personalized therapy based on an individual's genetic makeup. Identifying particular genetic changes linked to the illness can help with early detection, risk assessment, and ultimately the development of tailored medicines or interventions

Keywords: - The ABCC8-3C > T (rs1799854) variation was found to be significantly associated with T1DM ($p<0.01$) and “CT” genotype was found to be predominant in T1DM with a threefold increased risk to diabetes and the association was statistically significant. but we did not observe any significant association of G>A (rs5215) polymorphism of KCNJ11 with T1DM. Further ENSA C>T (rs1053732) variation was found to be significantly associated with T1DM ($p<0.01$).

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