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Title: First Comprehensive In Silico Analysis of the Functional and Structural Consequences of SNPs in Human GalNAc-T1 Gene

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Abstract: GalNAc-T1, a key candidate of GalNAc-transferases genes family that is involved in mucin-type O-linked glycosylation pathway, is expressed in most biological tissues and cell types. Despite the reported association of GalNAc-T1 gene mutations with human disease susceptibility, the comprehensive computational analysis of coding, noncoding and regulatory SNPs, and their functional impacts on protein level, still remains unknown. Therefore, sequence-and structure-based computational tools were employed to screen the entire listed coding SNPs of GalNAc-T1 gene in order to identify and characterize them. Our concordant in silico analysis by SIFT, PolyPhen-2, PANTHER-cSNP, and SNPeff tools, identified the potential nsSNPs (S143P, G258V, and Y414D variants) from 18 nsSNPs of GalNAc-T1. Additionally, 2 regulatory SNPs (rs72964406 and #x26; rs34304568) were also identified in GalNAc-T1 by using FastSNP tool. Using multiple computational approaches, we have systematically classified the functional mutations in regulatory and coding regions that can modify expression and function of GalNAc-T1 enzyme. These genetic variants can further assist in better understanding the wide range of disease susceptibility associated with the mucin-based cell signalling and pathogenic binding, and may help to develop novel therapeutic elements for associated diseases.

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