Structural and Dynamical Characterization of an α-1,6-Fucosyltransferase

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Fucosyltransferases catalyze the transfer of a fucose residue to a glycoconjugate. In mammalian organisms, this type of fucosylation can be related to a wide diversity of biological processes, including blood antigens, cell adhesion and also severe diseases such as cancer metastasis. FUT8 is an α-1,6-fucosyltransferase responsible for transferring a fucose residue from a donor substrate (GDP-β-L-fucose) to a N-acetylglucosamine of the core structure of a N-linked glycan. Deletion of this fucose in proteins promotes a type of human congenital disorder of glycosylation. Also, the level of core fucosylation is found to be elevated in hepatocarcinogenesis. In this context, the present work intents to study the dynamics of FUT8 in aqueous solution and bound to its substrate, GDP-β-L-fucose. Accordingly, FUT8 (PDBID 2DE0) was submitted to molecular dynamics simulations using the GROMACS simulation suite and GROMOS96 53a6 forcefield. Parameters for GDP-β-L-fucose were built combining parameters described in the forcefield for ATP, guanine and also parameters previously described by our group for fucose. The so obtained data demonstrate that the dynamic behavior of FUT8 is modulated by the enzyme’s substrate binding to the putative catalytic site. These data will be employed in docking studies between FUT8 and the fucose acceptor, the N-linked glycan. We expect that the dynamical characterization of FUT8 will offer original insights for this enzyme role on pathological process and, consequently, to potential new therapeutical strategies.

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