Protein-Carbohydrate Interactions Assessed through Molecular Dynamics Simulations Using the GROMOS Force Field

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INTRODUCTION. Carbohydrates have been increasingly associated with several biological events, from immune defense to cellular growth, and to influence a broad range of protein properties, as folding and stability. A proper understanding of carbohydrate roles over biological systems requires an appropriate characterization, at the atomic level, of their conformation, dynamics and interaction to target molecules. In this scenario, atomistic molecular dynamics simulations emerge as a powerful tool, providing data about carbohydrates and protein-carbohydrate complexes typically inaccessible to experimental methods, with both atomic and temporal resolution. OBJECTIVES: Considering the above mentioned data, the present work intends to evaluate how protein-carbohydrate interactions influence polypeptides conformation, dynamics and function. MATERIALS AND METHODS. This work performed unbiased molecular dynamics (MD) simulations using GROMACS simulation suite, and GROMOS 43A1, 53A6, 53A6$_{GLYC}$ and 54A7 force fields for the studied protein and carbohydrate moieties. RESULTS AND DISCUSSION. When covalently bound to a polypeptide as a glycoprotein, carbohydrates are observed to significantly reduce the flexibility of protein regions three-dimensionally close to the glycosylation site, as in human protectin and plant extensins, in accordance to wet lab experiments. Moreover, glycan chains may promote conformational changes that alter the function of enzymes, as human glucocerebrosidase and human thrombin. In the case of non-covalent protein-carbohydrate binding, MD simulations may help determining the molecular basis to explain why similar protein structures, as human thrombin and factor Xa, can differentially interact with the same polysaccharide, but be both functionally influenced by this binding. CONCLUSIONS: The GROMOS family of force fields is capable to adequately describe glycoproteins and protein-carbohydrate complexes conformation and dynamics, in accordance to previous experimental data, also supporting atomic-level interpretations of biochemical and functional data.

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