Dynamics of Lipid-Linked, Membrane Soaked, Oligosaccharides: Biological Precursors for N-Glycosylation in Eukarya and Prokarya

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INTRODUCTION: Lipid-linked oligosaccharides (LLOs) are the substrates of oligosaccharyltransferases (OSTs), enzymes that catalyzes the *en bloc* transfer of the oligosaccharide during the process of N-glycosylation. LLOs are composed by an isoprenoid moiety and an oligosaccharide, linked by a pyrophosphate group (PP). LLO lipid component is a dolichol in eukarya and undecaprenol in prokarya. Additionally, the number of isoprene units may change between species. **OBJECTIVE:** To obtain models for eukarya and prokarya LLOs soaked in biological membranes, able to describe their 3D structure and dynamics, as a previous and required step to further studies of their complexation and processing by OSTs. **MATERIAL AND METHODS:** We employed the GROMOS53A6 force field, added by GROMOS GLYC parameters for the saccharidic moiety. Starting glycosidic linkage geometries were based on energy contour maps derived from metadynamics in SPC solvent. The torsional parameters for the isoprenoid portion were derived from a fit to the proper quantum mechanical potential energy profiles at the HF 6-31G* and validated against experimental condensed phase properties. Molecular dynamics simulations employed GROMACS package for access the orientation, structure, and dynamics of eukaryotic (Glc3-Man9-GlcNAc2-PP-Dolichol) and bacterial (Glc1-GalNAc5-Bac1-PP-Undecaprenol) LLO in POPC and POPE bilayers, respectively. **RESULTS AND DISCUSSION:** The obtained topologies for isoprenoid group was able to properly reproduce experimental thermodynamic properties such as enthalpy of vaporization and density. The MD simulations of both LLOs revealed that most carbohydrate residues stay above the membrane lipid head groups, the PP linkages are within the lipid head group, and the isoprenoid chains are within the bilayer. Overall, there are similar orientations, structure, and dynamics of eukaryotic and bacterial LLOs in bilayers. **CONCLUSIONS:** The preferred orientation, structure and dynamics of LLOs provided information for complexation by OSTs, allowing further studies of how the OST PglK catalyzes the translocation of LLO across the membrane and how the oligosaccharide chain is transferred to a protein by OST PglB.

Keywords: LLO, N-glycosylation, molecular dynamics.
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