سمینار هفتگي ماده چگال نرم

GAG Positioning on IL-1RI; a Mechanism Regulated by Dual Effect of Glycosylation

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چکیده

IL-1RI is a glycosylated transmembrane receptor for the IL-1 family of cytokines that is involved in establishment of the innate and acquired immune systems. Extracellular domain of the IL-1RI binds to agonist such as IL-1β or antagonist ligands and the accessory protein to form the functional signaling complex. Dynamics and ligand binding of the IL-1RI is influenced by presence of the glycosaminoglycans (GAGs) of the extracellular matrix. Here a combination of molecular dockings and molecular dynamics simulations of the glycosylated and unglycosylated IL-1RI extracellular domain in the apo, GAG-bound and IL-1β-bound states were carried out to explain the co-occurring effect of receptor's glycosylation and GAGs. It was shown that the IL-1RI adopts two types of "extended" and "locked" conformations in its dynamical pattern and glycosylation maintains the receptor in the latter form. Maintaining the receptor in the locked conformation disfavors IL-1β binding by burring its two binding site on the IL-1RI extracellular domain. Glycosylation disfavors GAG binding to the extended IL-1RI extracellular domain by sterically limiting the GAGs degrees of freedom in targeting its binding site. While it favors GAG binding to the locked IL-1RI by favorable packing interactions.

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