In Silico Study of Ligand Binding Site of Toll-Like Receptor 5

Nastaran Sadat Savar[1]; Saeid Bouzari*[2]

1- Science and Research Branch,Islamic Azad University,Tehran, Iran

2- Department of Molecular Biology, Institute Pasteur of Iran,Tehran, Iran

saeidbouzari@yahoo.com

Background & Objectives: Toll-like receptors (TLRs) constitute an important family of innate immune receptors that recognize pathogen-associated molecular patterns(PAMPs). Bacterial flagellin (FliC), the major structural protein of flagellar filament, considers as one of the PAMPs and can be detected by the innate immune system via activation of TLR-5 which signals through nuclear factor kappa B (NF-κB) induces transcription of pro-inflammatory cytokines. In silico study of the interaction between FliC and TLR-5, could lead us toward the prediction of binding sites and the mechanism of agonist recognition by TLR5.

Methods: Tertiary structures of human TLR-5 and *Salmonella typhimurium* FliC were determined from RCSB protein data bank (PDB). Truncated structures of TLR-5 were designed based on the interaction sites to find the most critical region for interaction. The interactions of the full native TLR-5 and the truncated forms with FliC were evaluated using Hex docking server. Minimizations and visualizations were carried out by ViewerLite 4.2 and Swiss pdbViewer 4.0.

Results: The binding affinities and the poses of the interactions were investigated and in silico analysis revealed that one amino acid sequence within the central region of TLR-5 has the most suitable interaction with FliC and its free energy was compatible with that of TLR-5 full length original form.

Conclusion: According to our in silico results, the binding site is located in the central region of TLR-5 and this finding is well supported by previous experimental studies. This study provides the structural analysis for TLR-5/agonist interaction that may guide future studies in this important area

Keywords: In Silico Study; Toll-like Receptor5; Ligand Binding Site