In-silico modification of recombinant interleukin-18 for binding affinity prediction towards its binding receptor

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Abstract: Cancer is a common cause of death worldwide. Various methods were introduced as efficient treatments including immunotherapy. Immunotherapy deals with an application of functional protein to boost immune system for cancer elimination. An immunotherapeutic protein called interleukin-18 (IL18) has caught our interest due to its efficiency for natural killer cell and cytotoxic T lymphocyte promotion as well as metastasis inhibition. In this work we have used molecular dynamics simulation (MD) and protein-protein docking to predict potential mutation point. Since IL18 binds interleukin-18 receptor alpha (IL18a) to perform an action, the alteration of amino acid in IL18 could play a key point. Some mutations such as N91K and N111K were selected based on a structure of IL18-IL18Ra (PDB code 3WO3). We also choose our previously published recombinant E6K-T63A and wild type protein (WT) as comparative controls. MD simulation with AMBER16 force field with 310 K (37 °C) and 1 atm of IL18 in 0.15M NaCl solution was modelled to mimic cellular environment. We found E6K-T63A and N111K provide better binding to IL18Ra, compared to WT-IL18. It implied the higher affinity of N111K. This can lead to novel alteration of interleukin-18 and shorten time and budget for further improvement.

Keywords: Interleukin-18; Immunotherapy; Protein-protein docking; Molecular dynamics simulation; Recombinant protein