4.4.1 protein preparation Firstly, we will choose the best crystal structure of PD-L1 from the protein data bank with (PDB ID: 8P64) based on its co-crystallized ligand, clear binding site, and appropriateness for docking validation (Sastry et al., 2013),For protein preparation to be performed, we will use the Protein Preparation Wizard tool within the Maestro software in order to prepare the protein appropriately for subsequent molecular docking and simulation procedures(Schrodinger, 2023;Sastry et al., 2013) .All the usual preparatory steps will be carried out: adding missing hydrogen atoms, adjusting protonation state at an approximate pH of 7.4 using PROPKA, assigning correct bond orders, removing and retaining necessary water molecules likely to take part in binding or retaining a presumed bound water molecule once analyzed into place, fixing up added missing side chain atoms (or geometry) after reconstruction with the Prime module, and optimizing the H-bond network.4.4 Molecular Docking The Glide module incorporated in Maestro will be used for molecular docking (Friesner et al., 2004).Hierarchical VS protocol, HTVS (High-Throughput Virtual Screening), SP (Standard Precision) and XP (Extra Precision) will be followed.The priority on the docking scores and binding postures to be afforded upon compounds after docking should been assigned.(Friesner et al., 2004).A reference ligand present in the original crystal structure (co-crystallized ligand) will be re-docked into the binding site to assess and validate the docking protocol.(Halgren et al., 2004).Ionization states will be produced at pH 7 +- 2 and relevant tautomers and stereoisomers will be produced if necessary,The energy-minimized using the OPLS3e force field45 and keeping only heavy atoms at 150A MD cutoff structures will be used for molecular docking (Sastry et al., 2013).4.6 Molecular Dynamics Simulations Molecular dynamics simulations will be performed to assess the stability of computationally selected PD-L1-ligand complexes.

Summarized by © lakhasly.com