Design, Molecular Dynamic Simulation and Docking of An Anti-angiogenic Peptide

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Abstract: Angiogenesis is an essential process for the growth of solid tumors. The suppression of any phases of angiogenesis inhibits the formation of new vessels thus influencing tumor growth and metastasis [1]. One group of growth factor receptors critically implicated in angiogenesis is vascular endothelial growth factor receptors (VEGFR-1, -2, and -3), a subfamily of receptor tyrosine kinases (RTKs) [2]. Development of VEGF-Rs antagonists, which inhibit these molecules interacting with their ligands, is a validated therapeutic strategy of anti-cancer treatment. In the present study, we designed an antagonistic peptide based on the crystal structure of ligand in complex with VEGFR-1 considering critical residues in receptor-ligand interaction. A three-dimensional (3D) model of the peptide was constructed using homology modeling in MODELLER, version 9.16. One structure was chosen out of 10 models and subsequently subjected to the energy minimization. Molecular dynamics (MD) simulation was applied to allow conformational relaxation of the structure before being subjected to the docking procedure. Docking process of the peptide and VEGFR-1 was performed through HADDOCK webserver. As expected, van der Waals and nonpolar interactions played the most important role in ligand-receptor binding and the peptide has a similar binding site like native ligand. Regarding the results of docking and MD simulation, this study provides a novel discovery in the design and development of anti-angiogenic peptides for the delivery to cancer cells.

Keywords: Angiogenesis; Cancer; anti-angiogenic peptide; MD simulation; Docking

References

[1] L. D'Andrea, A. Del Gatto, "Peptide-based Molecules in Angiogenesis," Chem Biol Drug Des, 67(2006) 115–126.

[2] N. Rahimi, "Vascular endothelial growth factor receptors: Molecular mechanisms of activation and therapeutic potentials," 83(5) (2006) 1005–1016.