Molecular Dynamic Simulations of the Estrogen Receptor Alpha

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Abstract

Estrogen receptors are known as nuclear receptors. They exist in the cytoplasm of human cells and serves as a DNA binding transcription factor, which regulates gene expression. However the estrogen receptor also has additional functions independent of DNA binding. The human estrogen receptor comes in two forms, alpha and beta. This work focuses on alpha form of the estrogen receptor. The ER is found in breast cancer cells, ovarian stroma cells, endometrium, and the hypothalamus. It has been suggested that exposure to DDE, a metabolite of DDT, and other pesticides causes conformational changes in the estrogen receptor. Before examining these factors exclusively, this work examines the protein unfolding from the antagonist form found in the 3ERT PDB crystal structure, which has the estrogen receptor, bound to the cancer drug 4-hydroxytamoxifen. The conformational change exposes the binding clef of the co-peptide beside Helix 12 of the receptor forming the agonist conformation. Two key conformations in the loops at either end of the H12 produce the antagonist to agonist conformation. The results were generated a 42ns Molecular Dynamics simulation using AMBER FF99SB.