Prediction and investigation of Role of a Hotspot Residue on active Site Properties of Human glandular kallikrein–2 (hk)-2 in Prostate Cancer

Samaneh ahmadzadeh[1], Rahman Emamzadeh[1], Mahboobeh Nazari[2]

[1]Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran
[2]Department of Recombinant Technology Research, Nanobiotechnology Research Center, Avicenna Research Institute (ACECR), Tehran, Iran

Sci_rahman@yahoo.com

Abstract

Prostate cancer is the second most diagnosed cancer of men all over the world. Rising levels of PSA in serum are associated with prostate cancer. This cancer is almost close to infertility. Prostate-specific antigen (PSA) is a protein produced by normal prostate cells. This enzyme participates in the dissolution of the seminal fluid coagulum and plays an important role in fertility. The highest amounts of PSA are found in the seminal fluid; some PSA escapes the prostate and can be found in the serum. Human glandular kallikrein (hK)-2 is a serine protease that has approximately 80% structural homology with prostate-specific antigen (PSA). It is responsible for the conversion of the inactive pro-PSA zymogen to the enzymatically active PSA. In this study, initially, the pdb structure (PDB ID:4FNE) of Human glandular kallikrein–2 (hk2) was obtained from www.PBD.com and then was submitted to Hotspot Wizard server. The obtained results were evaluated in order to find an amino acid with a high mutability which located at the mouth of the active site. Thus, Pro207 was chosen for further analysis. At first the three dimensional (3-D) structure of proPSA was taken from www.PDB.com . Homology modeling of glandular kallikrein–2 mutant containing P207A mutation was performed using 3-D model of native glandular kallikrein–2 (PDB ID: 4FNE) by SWISS-MODEL server. Then, molecular docking simulation was done using Molegro Virtual Docker 2010.4.1.0. The results indicated that this mutation cause decreasing in binding energy and it seems that P207A mutation play an important role in enzyme active site.

Keyword: Prostate cancer, PSA, Human glandular kallikrein (hK)-2, mutation, Molegro