سیویلیکا - ناشر تخصصی مقالات کنفرانس ها و ژورنال ها
گواهی ثبت مقاله در سیویلیکا
CIVILICA.com

عنوان مقاله:

Prediction and Investigation of Role of a Hotspot Residue on binding Site Properties of HER2 Inhibitor (Trastuzmab) in Breast Cancer

محل انتشار:

یازدهمین کنگره بین المللی سرطان پستان (سال: 1394)

تعداد صفحات اصل مقاله: 2

نویسندگان:

Samaneh ahmadzadeh - *Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran*

Mahboobeh Nazari - *Department of Recombinant Technology Research, Nanobiotechnology Research Center, Avicenna Research Institute (ACECR), Tehran, Iran*

Mahboobeh Nazari - *Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran*

خلاصه مقاله:

Introduction: The human epidermal growth factor receptor 2 (HER2) is a member of the erbB class of tyrosine kinase receptors. These proteins are normally expressed at the surface of healthy cells and play critical roles in the signal transduction cascade in a myriad of biochemical pathways responsible for cell growth and differentiation. However, it is widely known that amplification and subsequent overexpression of the HER2 encoding oncogene results in unregulated cell proliferation in an aggressive form of breast cancer known as HER2-positive breast cancer. Monoclonal antibodies (mAbs) are currently the fastest growing class of therapeutic proteins. The single-chain variable fragment (scFv) antibody is a minimal form of functional antibody comprised of the variable domains of immunoglobulin light and heavy chains connected by a flexible linker. Existing therapy such as trastuzumab (Herceptin®) scfv, a part of monoclonal antibody inhibitor is used in the treatment of HER2-positive cancers. Here, describe a targeted approach for affinity improvement of therapeutic antibodies. Material and methods: In this study, initially, the pdb structure (PDB ID:4x4x) of Herceptin scfv 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 binding site. Thus, Gly56 of chain D was chosen for further analysis. At first the three dimensional (3-D) structure of HER2 was taken from www.PDB.com. Homology modeling of Herceptin scfv mutant containing G56S mutation was performed using 3-D model of native Herceptin scfv (PDB ID: 4x4x) by SWISS-MODEL server. Then, molecular docking simulation was done using Molegro Virtual Docker 2010.4.1.0 and AutoDockTools-1.5.6. Results: The results indicated that this mutation with increase hydrogen bond between amino acids and improve binding affinity may cause increasing in binding energy and it seems that G56S mutation play important role in binding site of Herceptin scfv.

کلمات کلیدی:

Breast cancer, HER2, Herceptin scfv, Molegro, AutoDock

لینک ثابت مقاله در پایگاه سیویلیکا:

https://civilica.com/doc/726721