Kunan Bangphoomi 2013: Characterization of Single Domain-Antibodies and Small Molecular Inhibitors to ErbB2 Tyrosine Kinase. Doctor of Philosophy (Biochemistry), Major Field: Biochemistry, Department of Biochemistry. Thesis Advisor: Assistant Professor Kiattawee Choowongkomon, Ph.D. 163 pages.

Erythroblastosis oncogene B 2, also known as ErbB2, is a cell membrane surface-bound receptor tyrosine kinase protein that important for cell signaling pathway. ErbB2 protein overexpresses in ErbB2 positive cancer especially mammary cell cancer and lung cancer. Currently, trend of anti-cancer molecule is the development of target specific molecule such as lead compound and monoclonal antibody. Although, there are many anti-cancer drugs that launched in the market, the new candidate of anti-cancer drug is still important. In this study, the anti-cancer molecules including monoclonal antibody and lead compound were developed by using bio-panning and virtual screening technique. The VH/V_HH antibody against ErbB2-TK clone number 4, 17, 22, and 25 provided the ELISA binding signal with ErbB2-TK and EGFR-TK. Moreover, the VH/V_HH antibody clone number 4 and 22 can inhibit the TK activity of EGFR. The tetrad amino acid hallmark identification revealed that, the amino acid sequence analysis revealed that clone number 4, 22, and 25 were VH antibodies, while clone number 17 was V_HH antibody. The molecular docking of VH/V_HH antibody clone number 4, 17, 22, and 25 revealed that, there are many binding sites of all antibodies on ErbB2-TK and EGFR-TK. The docking results of all antibodies correlated with ELISA and inhibiting TK activity assay. In addition, the structure of ErbB2-TK was used to screen lead compound from NCI database and ChemBridge Diverset™. There are 10 lead compounds that analyzed the binding residue from each library.

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