Editorial

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Structure-based Drug Design and R & D for Anti-Tumor and Anti-Virus Small Molecules

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Introduction

In structure-based drug design, the basic goal is to design molecules that fit complementarily to a given binding pocket. Virtual screening is a cost-effective and efficient strategy in the identification of structural scaffolds and chemical moieties that are potentially important for binding to a target protein, provided a structural model of the protein target is available.

In the aspect of drug design, the applicant has firstly carried out a series of researches on the mapping method in 3D-QSAR. In the 3D-QSAR structure-activity relationship studies of the inhibitors of AIDS (AD) we found that the models based on docking conformation is better than the one based on common skeleton superposition after docking [1]. What is more, in the 3D-QSAR structure-activity relationship studies of the pyrrolopyrazoles inhibitors of aurora-A, the models based on docking conformation is better as well [2]. Furthermore, the 3D-QSAR study of ATR inhibitors showed that the model build by the stable conformation of inhibitors in molecular dynamics of the complexes after docking is better than the model build by the conformation of inhibitors in docking, suggesting a better over mapping method for building 3D QSAR model [3]. MM / GBSA has the advantage of fast calculation and accurate scoring, the studies on new AIDS target Vif and anti-tumor targets were conducted utilizing molecular dynamics simulation and MM / GBSA. Scoring functions are of great importance in drug design and virtual screening. To assess the performance of docking scoring function, FEP, MM-GBSA, and QM/MM-GBSA approaches, a series tests were conducted on PLK inhibitors. Vif is a novel target of HIV-1, which play an important role in HIV progressing. Since there was no protein-ligand complex structure as a reference, the structure-based drug design of Vif inhibitors is blocked. By blind docking, MD and MMGBSA, we found a reliable binding pocket C10a located in the BC area of Vif, the predictive value of this binding pattern is highly consistent with the experimental data (R2=0.941), providing a structural basis for the further design of novel small molecule inhibitors targeting vif [4]. When the protein-ligand complex structure of Vif was reported, two series of compounds were designed and synthesized as HIV-1 Vif inhibitors [5]. PI3Kα and mTOR are important targets for anti-tumor, by building 3D QSAR model, MD and MMGBSA energy decomposition, the selectivity was analyzed systematically, which provided a theoretical basis for the design of PI3Kα or mTOR small molecule inhibitors with high selectivity.

Bromodomain is a recognition module in the signal transduction of acetylated histone. BRD4, one of the bromodomain members, is emerging as an attractive therapeutic target for several types of cancer. A virtual screening against BRD4 containing pharmacophore generation, molecular docking, and MD simulation was conducted for novel anticancer agents, which is just accept in Chemical Biology & Drug Design. In recent years, series of coumarin derivatives were designed and synthesized as potential antitumor agents [6]. A few series of novel 2,3-dihydrochromeno[3,4-d]imidazol-4(1H)-one derivatives were designed and synthesized as potent anticancer cell proliferation and migration agents [7]. Another virtual screening was conducted for SQS inhibitors, which is accepted to publish on Journal of Chemometrics.

References

1 Li Z, Zhou M, Wu F, Li R, Ding ZY (2011) Self-organizing molecular field analysis on human beta-secretase onopeptide inhibitors:5,5-disubstituted aminohydantoins. Eur J Med Chem 46: 58-64.

2 He G, Qiu MH, Li R, Song XR, Zheng X, et al. (2011) Molecular docking-based 3D-QSAR studies of pyrrolo [3, 4-c] pyrazole derivatives as Aurora-A inhibitors. Mol Simulat 37: 31- 42.

3 Luo H, Shi JY, Lu LF, Wu F, Zhou M, et al. (2014) Molecular dynamics-based self-organizing molecular field analysis on 3-amino-6-

arylpyrazines as the ataxia telangiectasia mutated and Rad3 related (ATR) protein kinase inhibitors. Med Chem Res 23: 747-758.

4 Zhou M, Luo H, Li R, Ding ZY (2013) Exploring the binding mode of HIV-1 Vif inhibitors by blind docking, molecular dynamics and MM/GBSA. RSC Adv 3: 22532.

5 Meng Zhou, Rong-Hua Luo, Xue-Yan Hou, Rui-Rui Wang, Guo-Yi Yan, et al. (2017) Synthesis, biological evaluation and molecular docking study of N-(2-methoxyphenyl)-6-((4-nitrophenyl)sulfonyl)benzamide derivatives as potent HIV-1 Vif antagonists. Eur J Med Chem 129: 310-324.

6 Zhang WJ, Li Z, Zhou M, Wu F, Hou XY, et al. (2014) Synthesis and biological evaluation of 4-(1,2,3-triazol-1-yl)coumarin derivatives as potential antitumor agents. Bioorg Med Chem Lett 24: 799–807.

7 Xuan Han, Jiang Luo, Feng Wu, XueYan Hou, Guoyi Yan, et al. (2016) Synthesis and biological evaluation of novel 2,3-dihydrochromeno[3,4-d]imidazol-4(1H)-one derivatives as potent anticancer cell proliferation and migration agents. Eur J Med Chem 114: 232-243.