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Ligand-based screening for anti-dengue virus inhibitor

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Since *Dengue Virus* (DENV) infection causes epidemics in tropics/subtropics, sometimes it causes a potentially lethal complication, dengue hemorrhagic fever. Unfortunately, there are no effective drugs or vaccines against this infection. Thus, development of drugs and vaccines against DENV is expected. Recently, we found SK-12, a novel NS2/NS3 protease inhibitor, by structure-based *in silico* screening. In this study, we carried out some ligand-based *in silico* screening studies for improving the inhibitors based on the structure of SK-12. First, we defined a pharmacophore of SK-12, and then carried out a pharmacophore search using a compound database. Next, some fingerprints of SK-12 and of compounds in the same database were obtained and then a similarity search for the compounds was carried out. As the compound database, OCDD compound library provided by the University of Tokyo was used. All these calculations were operated by MOE (CCG Inc.). Finally, 80 compounds were extracted based on the docking score obtained by MOE Dock, from the compounds obtained by the above mentioned procedure. Viral replication assays and toxicity measurements of them by MTT assay showed that EC_{50}=0.51 μM for compound 1 (SK-12, EC_{50}=2.55 μM), which indicates that compound 1 is more active than SK-12. However, *in vitro* protease assay of compound 1 showed no inhibitory activities against NS2B/NS3. Then we tried to search the target molecules of compound 1, which might be the novel target molecules of anti-DENV inhibitor.

Biography

Tatsuya Takagi has completed his PhD from Osaka University. At that time, he had been an Assistant Professor of School of Pharmaceutical Sciences, Osaka University for 5 years. Then, since 1993, he had worked for the Genome Information Research Center, Osaka University as an Associate Professor until he became a Professor of Graduate School of Pharmaceutical Sciences, Osaka University in 1998. He has published more than 100 papers in reputed journals and serving as Chairman of Division of Structure-Activity Relationship of the Pharmaceutical Society of Japan.

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