Tatsuya Takagi, J Clin Trials 2018, Volume 8
DOI: 10.4172/2167-0870-C3-027

Tatsuya Takagi

Osaka University, Japan

SBDD of MDM2 and β-secretase inhibitors using FMO and machine learning

MDM2 (Mouse double minute 2 homolog) is known as a protein which is a significant negative regulator of p53. MDM2 is also considered to be E3 ubiquitin-protein ligase recognizing the N-terminal TAD (Transactivation Domain). Thus, MDM2-p53 interactions are proposed to be a promising therapeutic strategy for tumors. Previously, we reported a part of the FMO (Fragment Molecular Orbital) calculation results of MDM2 and its inhibitors at the 11th China-Japan Joint Symposium on Drug Design and Development. Although we showed a satisfactory result, we also thought the result could be improved using PIEDA (Pair Interaction Energy Decomposition Analysis). In this study, we added some FMO results and tried to obtain a better correlation using data mining methods, such as PLS. First, we selected significant 18 IFIE (Inter Fragment Interaction Energy) values and 45 electrostatic interaction energies as the results of PIEDA from 84 ones. Then we obtained two latent variables as the results of PLS and cross validations. Resulted scatter plot of the two latent variables. In this case, the best-squared correlation coefficient values between observed and calculated pIC50 of MDM2, 0.924, was obtained. FMO calculation results between β-secretase and inhibitors also will be shown.

Biography

Tatsuya Takagi has completed his PhD at the age of 32 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 150 papers in reputed journals and had served as Chairman of Division of Structure-Activity Relationship of the Pharmaceutical Society of Japan for three years (until March 2017).

Notes: