Naoto Motoyama et al., Med Chem (Los Angeles) 2017, 7:11 (Suppl)
DOI: 10.4172/2161-0444-C1-037

Interaction analysis of MDM2 inhibitor by fragment molecular orbital method

Naoto Motoyama[1], Tatsuya Takagi[1], Tian Yu-shi[1], Hirotomo Moriwaki[1] and **Norihito Kawashita[2]**
[1]Osaka University, Japan
[2]Kindai University, Japan

p53 protein, which has various kinds of functions such as angiogenesis inhibitor, DNA repair and apotosis, is a transcription factor controlling many gene groups. Among these gene groups, it is well-known that p53 is inhibitted by MDM2 (Mouse Double Minute 2 homolog), and mutation of p53 can cause cancer. Thus, it was proposed that inhibition of MDM2-p53 interactions must be a promising therapeutic anti-cancer strategy and some inhibitors have been reported. In this study, we calculated inter-fragment interaction energies (IFIE) of co-crystal structure of MDM2 with inhibitors by fragment molecular orbital (FMO) method and analysed the linearity between the calculated and the experimental intermolecular interaction energies. All calculations were conducted by the use of the structures after protonations, and energy minimizations of hydrogens by MOE2014. We used ABINIT-MP6.0+[1] for FMO calculations. Ab initio MP2 method and 6-31G* basis set were used. We calculated 18 structures and obtained a good correlation between sum of IFIEs and experimental inhibitory activities (R=0.780). In addition, we found some significant fragments for MDM2-inhibitor interactions. Moreover, we calculated some co-crystal structures of MDM2 with inhibitors of which co-crystal structures have not been published to PDB after changing some parts of inhibitor's structures. We also obtained a good correlation between predicted and experimental inhibitory activities. Thus, we concluded that FMO method is effective for *in silico* drug design.

Biography

Naoto Motoyama has completed his BS degree from Osaka University. Currently, he is pursuing his Postgraduate degree. He has participated in a reputed conference in Japan.

u449357i@ecs.osaka-u.ac.jp

Notes: