Alexander Heifetz, Med Chem (Los Angeles) 2017, 7:4 (Suppl)
DOI:10.4172/2161-0444-C1-029

6th World Congress on
MEDICINAL CHEMISTRY AND DRUG DESIGN
June 07-08, 2017 Milan, Italy

Alexander Heifetz

Evotec (UK) Ltd., UK

Accurate assessment of protein-ligand interaction energy in seconds with quantum mechanics

The understanding of binding interactions between any protein and a small molecule is a cornerstone of any efficient structure-based drug design (SBDD) process. X-ray crystallography and homology modeling are the main source of structural information required for rational SBDD. However, even with the crystal structure in hand, visual inspection and force field-based molecular mechanics calculations often used for the rationalization of ligand-protein potency cannot always explain the full complexity of the molecular interactions. Quantum mechanical (QM) approach was always considered as promising direction to achieve this goal, however; traditional QM is not feasible for large biological systems, due to their high computational cost. FMO method offers a considerable computational speed-up over traditional QM methods. One of the key features of the FMO approach is that it can provide a list of the interactions formed between the ligand and the receptor and a chemically intuitive breakdown of these interactions. Such information is essential for medicinal chemists to be able to rationally approach modification of lead compounds in order to increase favorable interactions. Recently, we have demonstrated that FMO can be even faster (sec instead of hours) without compromising the accuracy of the calculations by combining it with density-functional tight-binding (DFTB) method. We will demonstrate the prospective application of FMO method in drug-discovery programs and in study of ligand-receptor residence time.

Biography

Alexander Heifetz is a Principal Scientist at Evotec (UK) Ltd., a drug discovery services company and Visiting Scientist at University College London in the group of Professor Andrea Townsend-Nicholson. He has more than 15 years of experience in drug discovery industry and was involved in discovery of four clinical drug candidates for treatment of anxiety, major depressive disorder, pulmonary hypertension and Alzheimer's disease. He has more than 35 patents and 40 publications in the area of Medicinal Chemistry. In 2011, he received the Royal Society Industry Award for the development of methods for GPCR modeling. In 2001, he obtained his PhD from the Weizmann Institute of Science.

Alex.Heifetz@evotec.com

Notes: