MedChem & TDD 2017

18th International Conference on

MEDICINAL CHEMISTRY & TARGETEDDRUG DELIVERY

December 06-08, 2017 Dallas, USA

Keynote Forum

Day 1

Tatsuya Takagi, Med Chem (Los Angeles) 2017, 7:11 (Suppl)
DOI: 10.4172/2161-0444-C1-035

Tatsuya Takagi

Osaka University, Japan

SBDD of MDM2 inhibitors using FMO and data mining method

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 (trans activation domain). Thus, MDM2-p53 interactions is 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 Chem-Bio Informatics Society (CBI). However, we could not obtain sufficient correlation between calculated and observed activities of the inhibitors. In this study, we added some FMO results and tried to obtain better correlation using data mining methods, such as PLS. First, we selected significant 53 amino acids from 85 ones for interactions between MDM2 and inhibitors considering the IFIE values. Then we obtained two latent variables as a result of PLS and cross validations. Resulted scatter plot between observed and calculated pIC50 of MDM2 is shown in Figure 1. we could obtain better correlation coefficient, R2=0.879. We are now calculating PIEDA of the complexes.

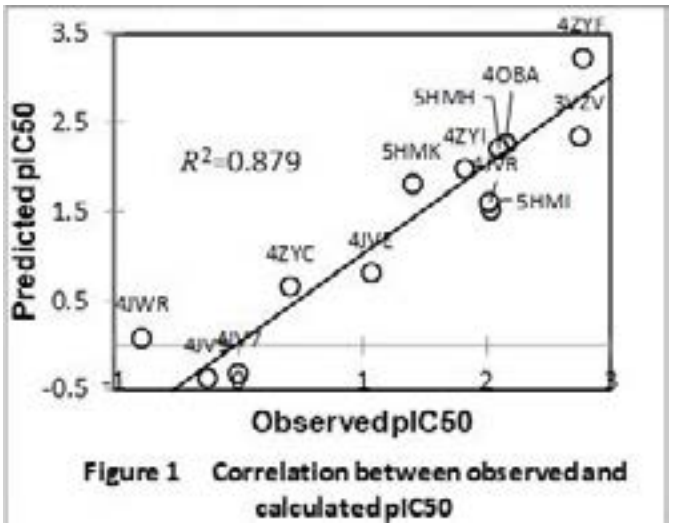

Figure 1 Correlation between observed and calculated pIC50

Biography

Tatsuya Takagi has completed his PhD from Osaka University. 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).

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Victor J Hruby, Med Chem (Los Angeles) 2017, 7:11 (Suppl)
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Victor J Hruby

University of Arizona, USA

Design of novel receptor selective bioavailable peptide and peptidomimetic ligands for G protein coupled receptors involved in major degenerative diseases

G-Protein Coupled Receptors (GPCRs) are targets for 30% of current drugs, but there are many unmet needs because these receptors and their ligands are intimately involved in many of our degenerative diseases. It has been difficult to obtain drugs that are effective and without side effects because there often are multiple subtypes of receptors and the endogenous hormones and neurotransmitters are non-selective. The 5 melanocortin receptors (MCRs) and the 3 opiate receptors (ORs) are important examples that are involved in many degenerative diseases, both central and peripheral. There is only 1 drug on the market for the MCRs, and the drugs on the market for the ORs are toxic and currently a great concern because of the drug overdose epidemic, which is costing billions and thousands of lives. To address this problem, we have developed a multimodal approach, using a combination of novel peptide and peptidomimetic scaffolds that address drug design in 3-dimensional space, with novel cyclic templates, computer assisted ligand/receptor interactions, orthosteric and allosteric agonist and antagonist activities, receptor selectivity and bioavailability for both the blood brain barrier and oral/transdermal availability. As time permits, we will illustrate this approach with design of melanotropin ligands that are highly selective agonists or antagonists for only 1 of the melanocortin receptors involved in pigmentary disorders, cancer, feeding and sexual disorders and neurodegeneration. For the opiate receptors, multivalent ligands that target opiate receptors and other receptors involved in pain pathways all in single ligands which do not have the toxicities of current opiates.

Biography

Victor J Hruby has received his PhD from Cornell University and has completed his Postdoctoral studies with Noble Laureate Vincent du Vigneaud. Currently, he is a Regents Professor at the University of Arizona, with major research interests in peptide hormones and neurotransmitters and their GPCR receptors, and their relationships to health and disease. He has over 1300 publications, chapters and reviews and over 25 patents. He has received numerous awards for his research, has been an editor and associate editor and on the Editorial Boards of several journals. He has served on several NIH Study Sections and been a consultant for many drug companies.

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Notes:

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Day 2

Mitsuji Yamashita, Med Chem (Los Angeles) 2017, 7:11 (Suppl)
DOI: 10.4172/2161-0444-C1-035

Mitsuji Yamashita

Shizuoka University, Japan

Preclinical researches on novel sugar dendritic Gd-DTPA MRI contrast agents and IER5/Cdc25B tageted phospha sugar antitumor agents to innovate in cancer therapy

Innovative and strategic materials against tumor cells to decrease sharply the number of dead people by tumors are desired eagerly. To innovate in medical technologies of diagnosis and cure for various kinds of tumors by novel medicinal materials, i.e., sugar dendritic Gd-DTPA complex MRI contrast agent (DEN-OH) and IER5/Cdc25B targeted novel phospha sugar antitumor agents (TBMPP) were prepared and evaluated *in vitro* and *in vivo* methods, and then these novel medicinal materials were revealed preclinically to have excellent characters against tumor cells.

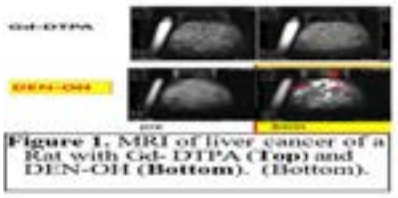

Figure 1. MRI of liver cancer of a Rat with Gd- DTPA (**Top**) and DEN-OH (**Bottom**). (Bottom).

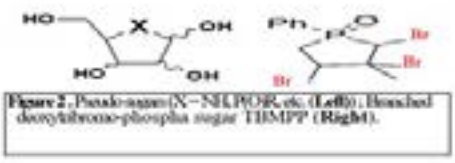

Figure 2. Pseudo-sugar (X=NH,POR, etc. (**Left**)), Brached deoxytibromo-phospha sugar TBMPP (**Right**).

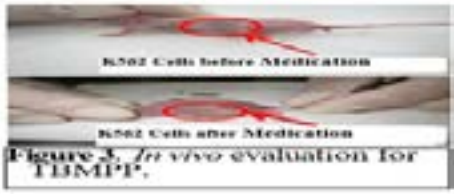

Figure 3. *In vivo* evaluation for TBMPP.

Biography

Mitsuji Yamashita has completed his PhD from Nagoya University, Japan, and Postdoctoral studies from Toyota Science and Chemistry Research Center, Japan, and Iowa State University, USA, as well as a Visiting Professor of University of Massachusetts, USA, and a Visiting Researcher of Oxford University, UK. He was a Professor of Shizuoka University, Japan, and he is now a Professor, Emeritus. He has published more than 180 papers and patents.

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