MedChem & CADD-2013
2nd International Conference on
Medicinal Chemistry & Computer Aided Drug Designing
October 15-17, 2013 Las Vegas, USA

Research and development on novel antitumor agents: Preparation, evaluation, and mechanism of low-molecular-weighted phospha sugar derivatives as IER5/Cdc25B targeted antileukemic agents

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Abstract

One of the most serious diseases today is cancer which causes the largest number of human die, nevertheless molecular targeted drugs are developed and used clinically. In this research novel multiple type molecular targeted antitumor agents of phospha sugar derivatives were investigated.

Sugar derivatives, whose oxygen atom in the hemiacetal ring is replaced by a nitrogen atom, etc., are called as pseudo sugars. These pseudo sugars of naturally occurring products such as aza sugars are well investigated to exert bioactivities. One the other hand, phospha sugars which have a phosphorus atom in the hemiacetal ring are not yet so well studied, nevertheless sugar derivatives and organo-phosphorus compounds play important roles in the living being.

Apart from the previous methodologies for preparing pseudo sugars based on sugar chemistry, we have prepared various phospha sugars by new methodologies starting from phosphorus heterocyclic compounds, mainly 2- and 3-phospholene derivatives, to construct the library of phospha sugars. Among the phospha sugars prepared branched di- and tri-bromo deoxyphospha sugar derivatives (DBMPP and TBMPP) as well as some substituted phospha sugar analogues were evaluated by MTT *in vitro* method, and characterized by flow cytometry and Western blotting to develop novel low-molecular-weighted antitumor agents. The phospha sugar derivatives enhanced the representation of IER5 and then suppressed the representation of Cdc25B, which is a common factor to accelerate the cell cycle of tumor cells. Therefore, we are expecting that phospha sugars may be developed to be multiple type molecular targeted antitumor agents with wide spectra targeting IER5/Cdc25B.

Biography

Mitsuji Yamashita has completed his PhD at the age of 27 years from Nagoya University, Japan, and postdoctoral studies from Toyota Science and Chemistry Research Institute, Japan, and Iowa State University. He was a professor of Graduate School of Science and Technology and retired at the age of 65 years old, and he is now an emeritus professor and specially-appointed professor of Shizuoka University, Japan. His research field is now focused on Medicinal Materials based on chemistry of carbohydrate and heterocycles. He has published more than 170 papers and patents as well as four books.