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**Innovative and strategic materials for medical technology against tumors: Preclinical researches on sugar dendritic Gd-DTPA complex MRI contrast agents and IER5/Cdc25B targeted novel phospho sugar antitumor agents**

Novel and high sensitive sugar dendritic Gd-DTPA complexes for tumor diagnosis and novel multiple type and wide spectral antitumor agents of low-molecular-weight phospho sugar derivatives which target IER5/Cdc25B to innovate in chemo-therapeutic treatments against various type of cancer cells were investigated. Sugar dendritic Gd-DTPA complex DEN-OH was prepared. The in vivo evaluation of DEN-OH for MRI contrast agent showed quite clear images of blood vessels as well as very early stage of cancer. Phospho sugars having a phosphorus moiety in the hemiacetal ring of the Haworth equation of sugars were prepared from phosphorus heterocycles by new synthetic methods to construct the compound library. And their preclinical evaluations and mechanistic investigations were carried out. Branched deoxybromo-phospho sugar derivatives such as DBMPP and TBMPP were found to exert novel, potential, and wide spectral antitumor activities by MTT in vitro evaluation method. The characterization and mechanism elucidation of these phospho sugar derivatives by flow cytometry and Western blotting showed that DBMPP and/or TBMPP enhanced the expression of cancer suppressors and suppressed the expression of cancer accelerators. TBMPP showed very high antitumor activity against blood cancer cells (K562, U937, etc.) as well as solid cancer cells and the IC<sub>50</sub> value against various kind of leukemia cells were almost the same values. TBMPP enhanced the expression of IER5 and then suppressed the expression of Cdc25B, which is the common and essential factor to act at the mitosis stage of tumor cell cycles. Therefore, phospho sugar derivatives might induce apoptosis at G2/M stage and inhibit the proliferation of various kinds of cancer cells (or stem cells of leukemia might be attacked by phospho sugars). In vivo evaluation for TBMPP against K562 cells transplanted to a nude mouse implied successful cure of cancer. Based on the preclinical research and computer aided drug designing we are expecting that phospho sugars may be developed to be clinically useful novel and innovative antitumor agents.

**Biography**

Mitsuji Yamashita has completed his PhD in 1972 from Nagoya University, Japan, and Post-doctoral studies from Toyota Science and Chemistry Research Center, Japan, and Iowa State University, USA. He was a visiting professor of University of Massachusetts at Amherst, USA, and a visiting researcher of Oxford University, UK, in 1994. He started his studies on phospho sugars in 1973 and promoted to be a Professor of Shizuoka University, Japan, in 1996 and retired at the age of 65 years to be a professor emeritus of Shizuoka University, Japan. His research field is now focused on medicinal materials based on chemistry of carbohydrates and phosphorus compounds to develop phospho sugar antitumor agents and sugar dendritic Gd-DTPA MRI contrast agents so as to be clinical use for innovating in cancer therapy. He has published more than 180 papers and patents as well as four books.

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