



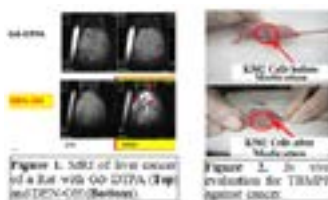
Mitsuji Yamashita

Shizuoka University, Japan

Innovative and strategic materials against cancer: Preclinical researches on tumour accumulative novel sugar dendritic Gd-DTPA complex MRI contrast agents and IER5/Cdc25B targeted novel phospho sugar anti-tumour agents to innovate in cancer therapy

Innovative materials against tumour to decrease remarkably the number of persons died by cancer are desired eagerly. To innovate in the medical technologies, tumour accumulative sugar dendritic Gd-DTPA complex MRI contrast agent (DEN-OH) and IER5/Cdc25B targeted novel phospho sugar anti-tumour agents (TBMPP) were prepared and evaluated preclinically. These novel medicinal materials were revealed to exert excellent characteristics against tumour cells. DEN-OH was prepared by introduction of protected sugar dendritic parts to the ligand of diethylenetriamine pentaacetic acid (DTPA) and the successive complex formation with Gd (III) and hydrolysis. The prepared DEN-OH for MRI contrast agent with the less concentration (10% Gd concentration of Gd-DTPA complex) showed quite clearer images of quite early stage (ca. 1 mm size) cancer (Figure 1). Phospho sugar derivatives were prepared by new synthetic pathway to construct the compound library. Deoxybromophospho sugar derivatives such as TBMPP (Tribromophospho sugar

derivative) prepared from phospholene derivative were first found to exert quite strong and wide spectral antitumor activities by in vitro evaluation against various kinds of leukemia cells such as K562, U937, etc. cell lines as well as solid cancer cells. Mechanistic studies with TBMPP against leukemia cells by Western blotting showed that the phospho sugar enhanced the expression of IER5, suppressed the expression of Cdc25B against tumour cells selectively and specifically, and then induced apoptosis at the mitosis step of the tumour cell cycle. In vivo evaluation for TBMPP was successfully performed by using a nude mouse transplanted by K562 cells on the skin (Figure 2).



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, USA. He was a visiting Professor of University of Massachusetts, USA and a researcher of Oxford University, UK in 1994. He was promoted to be a Professor of Shizuoka University, Japan in 1998 and retired at the age of 65 years old. He is now a Professor emeritus of Shizuoka University, Japan. He has published more than 185 papers, patents, and books.