Abstract

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. To innovate in the medical technologies, tumour accumulative sugar dendritic Gd-DTPA complex MRI contrast agent (DEN-OH) and IER5/Cdc25B targeted novel phospha sugar antitumour 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. To innovate in the medical technologies, tumour accumulative sugar dendritic Gd-DTPA complex MRI contrast agent (DEN-OH) and IER5/Cdc25B targeted novel phospha sugar antitumour 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). Phospha sugar derivatives were prepared by new synthetic pathway to construct the compound library. Deoxybromophospha sugar derivatives such as TBMPP (Tribromophospha sugar derivative)

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 phospha sugar enhanced the expression of IER5, suppressed the expression of Cdc25B against tumour cells selectively and

tumour cell cycle. Invivo evaluation for TBMPP was successfully performed by using a nude mouse transplanted by K562 cells on the skin. The main strategy to achieve a targeted CA relies on the optimization of each component, for example, the Gd3+ chelate unit, responsible for the imaging and the targeting moiety, responsible for the recognition

translation to routine use in clinic application a demanding process. Such parameters include: the thermodynamic

pharmacokinetic properties and good clearance, while guarantying an adequate imaging window; no in vivo toxicity