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Pharmaceutical Chemistry & Pathology Congress 2019: 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 phospha sugar anti-tumour agents to innovate in cancer therapy - Mitsuji Yamashita - Shizuoka University

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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 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. Phospha sugar derivatives were prepared by new synthetic pathway to construct the compound library. Deoxybromophospha sugar derivatives such as TBMPP (Tribromophospha 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 phospha 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.

Invivo evaluation for TBMPP was successfully performed by using a nude mouse transplanted by K562 cells on the skin.

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