conferenceseries.com SciTechnol

Hidetoshi Arima, J Pharm Drug Deliv Res 2017, 6:4 (Suppl)
DOI: 10.4172/2325-9604-C1-020

International Conference and Exhibition on

Nanomedicine and Drug Delivery

May 29-31, 2017 Osaka, Japan

Potential use of folate-appended methyl-β-cyclodextrin as a novel antitumor agent inducing mitophagy

Hidetoshi Arima
Kumamoto University, Japan

Methyl-β-cyclodextrin (M-β-CyD) induced apoptosis in tumor cells and had the potential as a novel antitumor agent and/or its lead compound. To obtain a tumor cell-selectivity of M-β-CyD, we newly synthesized folate-appended M-β-CyD (FA-M-β-CyD), and evaluated the potential of FA-M-β-CyD as a novel antitumor agent in vitro and in vivo. In contrast to M-β-CyD, FA-M-β-CyD entered KB cells (folate receptor (FR)-α (+)) through CLIC/GEEC endocytosis in a FR-β-dependent manner, and provided selective antitumor activity in FR-β-expressing cells by the induction of autophagy, not apoptosis. FA-M-β-CyD drastically inhibited the tumor growth after intratumoral or intravenous injection to FR-positive Colon-26 cells-bearing mice. Importantly, an intravenous administration of FA-M-β-CyD to tumor-bearing mice did not show any significant change in blood chemistry values. To gain insight into the detailed mechanism of this antitumor activity, we focused on the induction of mitophagy by the treatment of FR-β-expressing tumor cells with FA-M-β-CyD. The transmembrane potential of isolated mitochondria after treatment with FA-M-β-CyD was significantly elevated. Additionally, FA-M-β-CyD lowered ATP production and promoted reactive oxygen species production in KB cells (FR-α (+)). Importantly, FA-M-β-CyD enhanced light chain 3 (LC3) conversion (LC3-I to LC3-II) in KB cells (FR-α (+)) and induced PINK1 protein expression, which is involved in the induction of mitophagy. Furthermore, FA-M-β-CyD had potent antitumor activity in BALB/c nu/nu mice xenografted with KB cells (FR-α (+)) without any significant side effects. Taken together, these findings demonstrate that the autophagic cell death elicited by FA-M-β-CyD could be associated with mitophagy induced by an impaired mitochondrial function, and has the potential as a novel antitumor agent inducing mitophagy.

Biography

Hidetoshi Arima is working as a Professor at Graduate School of Pharmaceutical Sciences, Kumamoto University, Japan. He received a PhD in 1991 from Kumamoto University in Japan. From 1991 to 1993, he worked at Eisai Co., Ltd. in Japan. From 1993-1998, he worked at Tokyo University of Pharmacy and Life Sciences as Research Associate. In 1998, he moved to Faculty of Pharmaceutical Sciences in Kumamoto University in Japan, and then was promoted to Associate Professor in 2001. In 2007, he was promoted as Professor in Graduate School of Pharmaceutical Sciences, Kumamoto University in Japan. His research interest is design and evaluation of integrated drug delivery system (DDS) based on cyclodextrins. In addition, he started to research the potential use of sacran, a supergiant Cyanobacterial polysaccharide, as natural drugs and DDS carriers. He published over 150 research papers and 10 patents since 1986.

arimah@gpo.kumamoto-u.ac.jp

Notes: