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Tumor cell sensitization to anti-tumor agent-induced apoptosis

Cisplatin (V-diamminedichloroplatinum, CDDP) is a commonly used chemotherapeutic agent for the treatment of several solid tumors. CDDP binds to DNA to generate DNA adducts. CDDP regulates the activity of certain ion channels, transport proteins and various plasma membrane enzymes, and induces reactive oxygen species (ROS) during cancer chemotherapy. However, the precise mechanism underlying apoptosis of cancer cells induced by CDDP remains unclear. Specific gangliosides such as GM3, GD3, and GD1b induce apoptosis in various types of cells. GM3 treatment in immature proliferating glial and neuronal cells results in suppression of cell proliferation and the induction of apoptosis. Additionally, GM3 is involved in cell death through the accumulation of ROS and intracellular calcium ion influx into the neuronal cells. In murine bladder cancer cells, GM3 overexpression induces apoptosis and reduces malignant potential. Among the gangliosides, CDDP augmented the expression of only GM3 synthase and its product GM3. Reduction of the GM3 synthase level through ectopic expression of GM3 small interfering RNA (siRNA) rescued HCT116 cells from CDDP-induced apoptosis. This was evidenced by inhibition of apoptotic signals by reducing ROS production through the regulation of 12-lipoxygenase activity. Furthermore, the apoptotic sensitivity to CDDP was remarkably increased in GM3 synthase-transfected HCT116 cells compared to that in controls. In addition, GM3 synthase-transfected cells treated with CDDP exhibited an increased accumulation of intracellular ROS. These results suggest the CDDP-induced oxidative apoptosis of HCT116 cells is mediated by GM3.

Biography

Cheorl-Ho Kim has completed his PhD at the age of 28 years from The University of Tokyo and was positioned as a senior Scientist in Korea Research Institute of Bioscience and Biotechnology. He is a Professor of Molecular Glycobiology, Sungkyunkwan University, Korea, leading organization of Korea, which is cooperated with the SamSung Group. He has published more than 320 papers in reputed journals and serving as an editorial board member, executive editor and editor-in-chief of the international journals. His work was contributed to the mechanisms of glycan-mediated Hepatitis B viral oncogenesis and invasion, sialoglycan-mediated leukemic differentiation and vascular biology. He has been recognized as a pioneer expert in Molecular Hepatology, Glycobiology and Glycomics study, as evidenced and demonstrated by the following confirmations: The Lab has the authors of over 300 peer-reviewed articles published in international scientific journals.

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