Bo Yuan et al., J Cancer Sci Ther 2016, 8:9(Suppl)
http://dx.doi.org/10.4172/1948-5956.C1.085

Cytocidal effects of active bufadienolides on human cancer cells and its possibility of enhancing host immunity as an adjuvant therapeutic reagent

Bo Yuan[1], Jing H E[1], Keishi Kisoh[1], Hideki Hayashi[1], Sachiko Tanaka[2], Nan Sl[1], Hai-yu Zhao[1], Toshihiko Hirano[2], Baolin Bian[1] and **Norio Takagi[1]**
[1]Tokyo University of Pharmacy & Life Sciences, Japan
[2]China Academy of Chinese Medical Sciences, China

The growth inhibitory effects of bufadienolide compounds were investigated in a human glioblastoma cell line U-87 and a pancreatic cancer cell line SW1990. Among four bufadienolide compounds, a dose-dependent cytotoxicity was observed in these cancer cells after treatment with gamabufotalin and arenobufagin. The IC_{50} values of the two compounds were 3-5 times higher in normal peripheral blood mononuclear cells (PBMCs) than those in both cancer cells. However, similar phenomena were not observed in other two bufadienolide compounds, telocinobufagin and bufalin. These results thus suggested that gamabufotalin and arenobufagin possessed a selective cytotoxic activity against tumor cells rather than normal cells. Moreover, a clear dose-dependent lactate dehydrogenase (LDH) release, a well-known hallmark of necrosis, was observed in both cancer cells treated with gamabufotalin, suggesting that gamabufotalin-mediated cell death is predominantly associated with a necrosis-like phenotype. Of most importance, treatment with as little as 8 ng/ ml of gamabufotalin, even an almost nontoxic concentration to PBMCs, efficiently downregulated the percentages of $CD4^+CD25^+Foxp3^+$ regulator T (Treg) cells in mitogen-activated PBMCs. Given that Treg cells play a critical role in tumor immunotolerance by suppressing the antitumor immunity, these results suggested that gamabufotalin could be served as a promising candidate of adjuvant therapeutic reagent by manipulating Treg cells to enhance the efficacy of conventional anticancer drugs and less their side effects. These findings provide insights into the clinical application of gamabufotalin for cancer patients with glioblastoma/ pancreatic cancer based on its cytocidal effect against tumor cells as well as depletion of Treg cells.

Biography

Bo Yuan has completed his PhD from Tokyo University of Pharmacy and Life Sciences (TUPLS) and has done research at University of California, San Francisco as a Visiting Assistant Professor from 2009 to 2010 and is currently an Assistant Professor. His research interest focuses on the novel antitumor effect of clinically used antitumor drugs in combination with naturally occurring phytochemicals in terms of sensitization of cancer cells to drugs resulting in dosage reduction for clinical application. He has published more than 40 papers in reputed journals.

yuanbo@toyaku.ac.jp

Notes: