



Title: Induction of Cancer Cell-specific Cell Death and Alteration of Sugar Chain Synthesis Pathways by Low Molecular Weight Fucoidan Extract

Dr. Sanetaka Shirahata

Professor
Kyushu University
Japan

Abstract

Fucoidan is sticky fucose-rich sulfated polysaccharides derived from seaweeds such as *Konbu* or *Mozuku*. Low molecular weight fucoidan extract (LMWFE) digested by abalone glycosidases exhibited anti-invasion and anti-angiogenesis effects. LMWFE is now widely used for therapy of terminal cancer patients in Japan. Recently, we found that LMWFE induced cancer cell-specific cell death, which is enhanced by concanavalin A (Con A), a lectin recognizing mannose moiety of polysaccharides. LMWFE enhanced the Con A reactivity of human fibrosarcoma HT1080 cells but not of TIG-1 cells, human normal fibroblasts. An N-acetylglucosaminyl-transferase V (GnT-V) exhibits an important role on the formation of branch chain of β -1,6-GlcNAc and relates to invasion and metastasis of cancer cells. A transcription factor Ets-1 is also deeply related to invasion and metastasis via expression of extracellular matrix degradation enzymes. LMWFE suppressed the gene expression of GnT-V and Est-1 but did not affect the ER stress pathway, suggesting that LMWFE suppressed the malignant properties of cancer cells including alteration of sugar chain synthesis pathways and induced cancer-specific cell death. The combined use of LMWFE with cisplatin, an anti-cancer drugs, resulted in enhancement of apoptosis of HT1080 cells and inhibition of cell death of TIG-1 cells by cisplatin.

Biography

Upon completion of his doctorate on anti-cancer effect of antioxidants inducing DNA damage in food science and technology at the Kyushu University in 1978 he joined the faculty at Shokei Jr. College as Associate Professor where he performed research on DNA damage induced by tannins (Shirahata et al., 1985; Shirahata et al., 1989). In 1987 he visited Oregon State University and promoted research on the transformation of serum-free mouse embryo (SFME) cells by oncogenes (Shirahata et al., 1990; Rawson et al., 1991). In 1989 he joined the faculty of agriculture, Kyushu University as Associate Professor and established an oncogene-activated production system in which the CMV promoter was activated by *ras* oncogene to establish recombinant protein-high producers (Teruya et al., 1993). He also developed an *in vitro* immunization method to produce human monoclonal antibodies specific to cancer cells. In 1995, he was promoted to Professor, Faculty of Agriculture, Kyushu University and joined to the Graduate School of Systems Life Sciences in 2003. Dr. Shirahata directed research on electrolyzed reduced water, which inhibit tumor angiogenesis (Ye et al., 2008). He also revealed that enzyme-digested low molecular weight fucoidan extract inhibit invasion and angiogenesis of tumor cells (Ye et al., 2005). Recently he is collaborating with clinicians who are treating terminal cancer patients with the fucoidan extract.