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Inhibition of breast cancer bone metastasis and pancreatic and colon cancer by synthetic curcumin analogue UBS109

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Therapy of breast cancer metastasis with UBS109:An estimated 30% of women diagnosed with invasive breast cancer will have a recurrence and may eventually die of their disease. An estimated 90% of deaths due to breast cancer are a consequence of metastatic disease. Bone is one of the most common sites (70%) of metastasis.Monocarbonyl analogs of curcumin (MACs) include UBS109, EF31 and EF24. UBS109 inhibited bone destruction induced by triple-negative breast cancer (TNBC) MDA-MB-231 cells. UBS109 directly stimulates osteoblastogenesis and mineralization in bone marrow cells from normal nude mice *in vitro* and stimulates osteoblast activation in preosteoblastic cells. Furthermore,UBS109 suppresses the differentiation of osteoclast precursors into mature osteoclasts. UBS109 inhibited breast cancer in the bone, osteolysis by inhibiting osteoclast precursors and osteoclasts, but promotes new bone formation by stimulating osteoblast activation. Recently, we have demonstrated that UBS109 inhibited lung metastasis of the TNBC. Novel therapy for pancreaticand colon cancer using UBS109: Pancreatic ductal adenocarcinoma (PDA) is the fourth most common cause of cancer death, the overall 5-year survival for PDA is less than 5%, a median survival of 4–6 months. Pancreatic cancer (PC) has a high incidence of clotting complications. We tested the cytotoxic activity of UBS109, EF31, EF24, HSP90 inhibitor, gemcitabine (current treatment), Akt inhibitor and p38 MAPK inhibitor against four different PC cells.UBS109 and EF24 inhibited 100% at less than 1.25 μM, but others did not inhibit 100% at concentrations up to 20 μM. UBS109 and EF31(25 mg/kg, I.V.)/week for 3 weeks significantly inhibited MiaPaCa-2 xenografts in mice.UBS109 (25 mg/kg, I.V.)/week inhibited colon cancer (HT-29 and HCT-116) xenografts better than a combination of oxaliplatin (5 mg/kg) and 5FU (30 mg/kg) I.V.

Biography

Mamoru Shojiobtained his Medical Degree from the Hokkaido University, Japan, and completed internships at the US Naval Hospital, Yokosuka, Japan and the University of Pennsylvania in Philadelphia. He did his residency in Internal Medicine at the Lahey Clinic, Boston and fellowship training in Immunology at the Peter Bent Brigham and Robert Breck Brigham Hospitals (mentor, John R David, MD), Harvard Medical School in Boston, in Tumor Immunology at the University of Minnesota (mentor, Charles F Mckhann, MD from Massachusetts General Hospital) in Minneapolis, followed by fellowship in Hematology and Medical Oncology at Emory University (mentor, Charles M Huguley, Jr., MD).

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