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

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Curcumin (diferuloylmethane) is a β-diketone constituent of the turmeric. It is used as a spice to give a specific flavor and yellow color to curry. However, its clinical efficacy is poor because of its low solubility. He worked with professors Liotta and Snyder at the Chemistry department to synthesize a series of novel monocarbonyl analogs of curcumin (MACs) approximately 100 analogs including EF24, EF31 and UBS109. Dr. Shoji's laboratory and the NCI tested the analogs for the anticancer activity. The NCI determined the mean growth inhibitory concentration (GI-50) of EF24, curcumin and cisplatin on the NCI-60 cancer cell panel, which are 0.7 μM, 7.3 μM and 9.5 μM, respectively. MACs do not kill normal breast cells MCF-10A but kill all cancer cells tested (KB-3-1, TU212, MiaPaCa, SE-Mel-28, RPMI-7951, and MDA-MB- 231 cells) at concentrations (0-20 μM). MACs inhibit NF-κB by inhibiting IKK-α and IKK-β. UBS109 inhibited breast cancer metastasis and osteolysis by inhibiting osteoclasts precursors and osteoclasts, but promotes new bone formation by stimulating osteoblast activation. UBS109 and EF24 inhibited four pancreatic cancer cell lines 100% at less than 1.25 μM, whereas gemcitabine did not up to 20 μM. UBS109 significantly inhibited MiaPaCa-2 pancreatic cancer xenografts and colon cancer (HT-29 and HCT-116) xenografts in mice at 25 mg/kg, iv once a week better than a combination of oxaliplatin (5 mg/kg) and 5FU (30 mg/kg) iv.

Speaker Biography

Mamoru Shoji has developed synthetic monocarbonyl analogs of curcumin (MACs) out of the 100 synthetic analogs with Drs. DC Liotta, JP Snyder, BK Adams and other colleagues. He and his colleagues try to move the analogs for clinical trials.

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