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# Pathobiology and prevention of bone Loss caused by cancer chemotherapy

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Cancer chemotherapy often induces bone loss or osteoporosis in cancer patients and survivors; yet the underlying mechanisms remain unclear and currently no specific adjuvant treatments are available to reduce these side effects. This study characterized damaging effects and action mechanisms of commonly used anti-metabolites methotrexate (MTX) and 5-fluoruracil (5-FU) on bone formation and osteoporosis in rats, and investigating effects of supplementary treatments with clinically used antidote folinic acid and some nutraceuticals which are known to possess anti-inflammatory, anti-oxidant, and/or anti-resorptive properties. We found that MTX or 5-FU chemotherapy increases expression of proinflammatory cytokines (TNF-α, IL-1β, IL-6, RANKL) and attenuates Wnt/β-catenin signaling in bone and bone marrow stromal cells. MTX or 5-FU chemotherapy causes osteoporosis by reducing bone formation, decreasing pool of bone marrow osteoprogenitor cells and differentiation of bone forming cells osteoblasts, enhancing adipocyte differentiation, increasing formation of bone-resorptive cells osteoclasts, resulting in bone loss and marrow adiposity. Supplementation with folinic acid attenuated MTX damaging effects on growth plate and production of primary bone. Oral doses of some nutraceuticals preserved osteoprogenitor cell content and bone formation, suppressed expression of osteoclastogenic factors in bone, osteoclast number on bone surface and bone resorption, and/or minimized accumulation of marrow fat. Sustaining/activating Wnt signaling by blocking its antagonist(s) also abrogated the bone defects. These observations suggest that cancer chemotherapy causes bone defects by damaging multiple compartments in the bone, and that some supplementary treatments may be beneficial in preserving bone integrity during chemotherapy.

## Biography

Prof Xian obtained his PhD in 1993 from Murdoch University (Australia). He has been interested in fundamental and strategic research into tissue growth, injury repair and roles of growth factors/cytokines and progenitor cells. His earlier research positions include those at Child Health Research Institute (Australia), University of North Carolina at Chapel Hill (USA), Flinders University, University of Adelaide and Women's and Children's Hospital (Australia). Since 2001, he has been leading his research group (currently at University of South Australia) conducting bone growth and repair research. He serves as Associate Editors for 4 journals and editorial board members for 8 international scientific journals.