Inhibitory Effect of Betulinic acid on RANK Ligand induced osteoclast differentiation

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樺木酸對 RANK Ligand 所誘導之破骨細胞分化產生之抑制效果

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Background: Osteoporosis is a condition where the bones thin and become weak and brittle. The bones also lose their density which causes slumping of the back. Many studies have proved that some inflammatory cytokines play an important role in the progression of osteoclastic differentiation. Betulinic acid, a main compound of traditionally used Chinese herb Forsythia, has anti-inflammatory activity. We tried to prove if the betulinic acid could be an inhibitor in the progress of osteoclast differentiation.

Methods: We used Raw264.7 macrophages treated with RANKL as our positive control. Then treat with betulinic acid with different concentrations. At last, we detected the proteins like JNK, ERK, p38, c-fos and NFATc-1 associated with osteoclastogenesis by western blot.

Results: Our study found that the betulinic acid markedly inhibited the receptor activator of nuclear factor kappa B ligand (RANKL) induced osteoclastic differentiation from RAW264.7macrophage cells. Tartrate-resistant acid phosphatase (TRAP) staining demonstrated that differentiation of osteoclast-like cells was inhibited in the presence of betulinic acid in a dose-dependent manner. Treatment of RAW264.7 macrophages with RANKL induced extracellular signal-regulated kinases (ERK), p38 and c-Jun N-terminal kinase (JNK) phosphorylation. We found that RANKL-induced ERK, p38 and JNK was attenuated by betulinic acid. The downstream of MAP Kinase, c-fos and NFATc-1 also involve in the osteoclast differentiation and also attenuated by betulinic acid.

Conclusions: Our data suggest that betulinic acid inhibits osteoclastogenesis from macrophage cells via attenuated of RANKL-induced ERK, p38 and JNK activation, which may protect bone loss from osteoclastogenesis.