学 位 論 文 の 要 旨

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主論文の題名

Inflammatory Skin-Derived Cytokines Accelerate Osteoporosis in Mice with Persistent Skin Inflammation

主論文の要旨

Secondary osteoporosis can also be caused by chronic inflammatory skin disease as well as rheumatoid arthritis or inflammatory bowel disease. However, the exact role of osteoporosis in inflammatory skin conditions has not been elucidated. Using a mouse model of dermatitis, we investigated the pathophysiology of osteoporosis in inflammatory skin conditions and the therapeutic impact of osteoporosis medication on inflammatory skin disease. We employed model mice of spontaneous skin inflammation, specifically overexpressing human caspase-1 in the epidermis. Bone density and the expression of various messenger ribonucleic acids (mRNAs) in the femur were examined by micro computed tomography (μCT) and real time polymerase chain reaction (RT-PCR). The effects of minodronate and anti- receptor activator of NF-κB ligand (RANKL) antibody on bone structure, histology, and femur blood flow were studied. The mouse model of skin inflammation showed a marked decrease in bone density compared to wild-type littermates with abnormalities in both bone resorption and formation. Minodronate improved bone density by decreasing osteoclasts, but anti-RANKL antibody did not improve. In the dermatitis model, the blood flow in the bone marrow was decreased, and minodronate restored this parameter. A model of persistent dermatitis exhibited marked osteoporosis, but the impact of chronic dermatitis on osteoporosis has not been thoroughly investigated. We should explore the pathogenesis of osteoporosis in skin inflammatory diseases.