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SYSTEMICALLY DELIVERED GLUCOCORTICOID LIPOSOMES SUPPRESS BONE EROSION AND INHIBIT OSTEOCLAST ACTIVATION IN SYNOVIUM AND BONE MARROW DURING EXPERIMENTAL MURINE ARTHRITIS

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Glucocorticoids are potent anti-inflammatory drugs that slow down the progression of bone erosion in patients with rheumatoid arthritis. By delivery of glucocorticoids encapsulated into long circulating liposomes, their anti-inflammatory effect over free drug can be increased. The aim of this study was to investigate the effect of systemic delivery of liposomal prednisolone phosphate (PLP) on bone erosion and osteoclast activity during experimental antigen-induced arthritis. Mice with established antigen-induced arthritis (AIA) were treated with a single intravenous injection of 10mg/kg

liposomal PLP, free PLP, phosphate buffered saline or empty liposomes. Knee joint inflammation and bone erosion were measured by histology and osteoclast activation by tartrate-resistant acid phosphatase (TRAP) staining and cathepsin K immunostaining. Direct effects of liposomal PLP on osteoclasts and bone resorption were measured in vitro on osteoclasts differentiated out of bone marrow cells with macrophage colony-stimulating factor (M-CSF) and RANKL.

Liposomal PLP strongly suppressed knee joint swelling, synovial infiltrate and bone erosion in AIA. The number of active osteoclasts was not only suppressed in bone lesions near inflamed synovium, but also within the trabecular bone of the tibia, suggesting a systemic suppression of osteoclast activation. Furthermore, liposomal PLP suppressed osteoclast differentiation factors M-CSF, RANK and RANKL in the synovium while it also directly blocked osteoclast differentiation and bone resorption in vitro. Targeting studies showed that liposomes are most efficiently phagocytosed by macrophages and early precursors of osteoclasts in the bone marrow rather than mature osteoclasts, suggesting a possible inhibition of osteoclast differentiation from an early stage.

Liposomal glucocorticoid delivery offers a more efficacious way to inhibit both inflammation and bone erosion in rheumatoid arthritis than free PLP.