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Folate-targeted liposomes for rheumatoid arthritis therapy

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Rheumatoid arthritis is the most common inflammatory rheumatic disease, affecting almost 1% of the world population [1]. Although the cause of rheumatoid arthritis remains unknown, the complex interaction between immune mediators (cytokines and effector cells) is responsible for the joint damage that begins at the synovial membrane [2]. Activated macrophages are critical in the pathogenesis of rheumatoid arthritis [3] and showed specifically express a receptor for the vitamin folic acid, folate receptor β [4]. This particular receptor allows internalization of folate-coupled cargo [5].
Here we propose the encapsulation of methotrexate in a new liposomal formulation using a hydrophobic fragment of surfactant protein conjugated to a linker and folic acid to enhance their tolerance and efficacy [6]. In this study we aim to evaluate the efficiency of this system to treat rheumatoid arthritis, by targeting folate receptor β present at the surface of activated macrophages. The specificity of our liposomal formulation was investigated both *in vitro* as *in vivo* using a mouse model of arthritis (collagen-induced arthritis in DBA/1J mice strain).
In both systems, the liposomal constructs were shown to be highly specific and efficient in targeting folate receptor β. These liposomal formulations also significantly increase the clinical benefit of the encapsulated methotrexate *in vivo* in arthritic mice (Figure 1) [7]. In conclusion, our formulation might be a promising cost-effective way to treat rheumatoid arthritis and delay or reduce methotrexate intolerance.

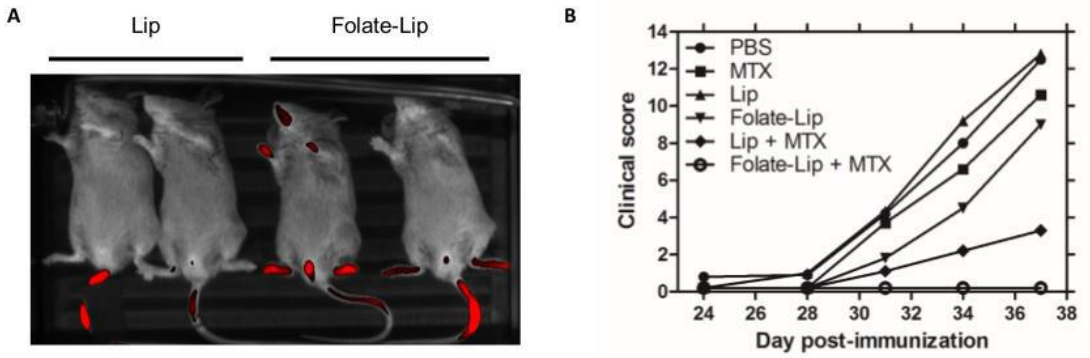

Figure 1. *In vivo* specific targeting and prophylactic efficiency of folate receptor-targeted liposomes in arthritic mice. (A) *In vivo* uptake specificity of fluorescently labeled liposomes (30 min). (B) Clinical effects of liposomes encapsulating methotrexate on arthritis. Treatment started 14 days after immunization. The mean clinical score in each group over time is shown [8].

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