A novel DNA vaccine targeting macrophage migration inhibitory factor protects joints from inflammation and destruction in murine models of arthritis.

OBJECTIVE: Previous studies have demonstrated that neutralization of macrophage migration inhibitory factor (MIF) by anti-MIF antibodies decreases joint inflammation and destruction in a type II collagen-induced arthritis model in mice. The aim of this study was to develop and describe a simple and effective method of active immunization that induces anti-MIF autoantibodies, which may neutralize MIF bioactivity.

METHODS: We developed a MIF DNA vaccine by introducing oligonucleotides encoding a tetanus toxoid (TTX) Th cell epitope into the complementary DNA sequence of murine MIF. Mice were injected with this construct in conjunction with electroporation. The ability of this immunization to inhibit the development of collagen antibody-induced arthritis (CAIA) in BALB/c mice and spontaneous autoimmune arthritis in interleukin-1 receptor antagonist (IL-1Ra)-deficient mice was then evaluated.

RESULTS: Mice that received the MIF/TTX DNA vaccine developed high titers of autoantibodies that reacted to native MIF. Compared with unvaccinated mice, vaccinated mice also produced less serum tumor necrosis factor alpha after receiving an intravenous injection of lipopolysaccharide. In addition, vaccination with MIF/TTX DNA resulted in significant amelioration of both CAIA in BALB/c mice and symptoms of autoimmune arthritis in IL-1Ra-deficient mice.

CONCLUSION: These results suggest that MIF/TTX DNA vaccination may be useful for ameliorating the symptoms of rheumatoid arthritis. (1)

Figure 5. Representative results of histologic analysis of the effects of vaccination with saline (A, D, and G), pcAGGS (B, E, and H), or macrophage migration inhibitory factor/tetanus toxoid (C, F, and I). Ankle joints from interleukin-1 receptor antagonist (IL-1Ra)-knockout mice were collected 16 weeks after vaccination, and specimens were stained with hematoxylin and eosin (A–C) or Safranin O (D–F), or were immunohistologically stained with polyclonal anti-MIF antibodies (G–I). (Original magnification 200.)