Tech-Trends

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DNA Vaccine Through In-Vivo Electroporation

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-knockout mice.

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

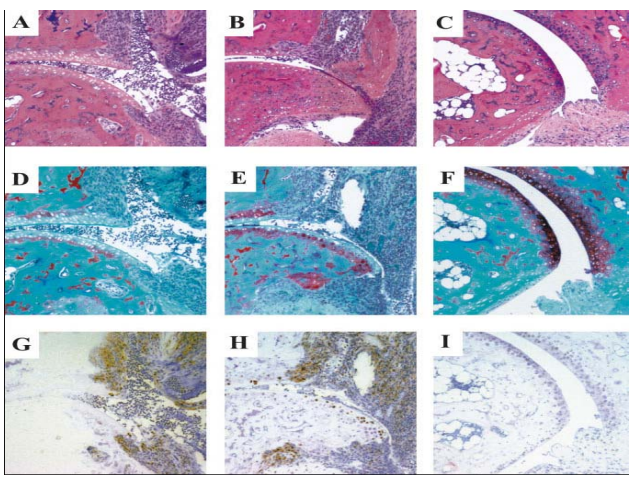

Figure 5. Representative results of histologic analysis of the effects of vaccination with saline (**A, D,** and **G**), pCAGGS (**B, E,** and **H**), or macrophage migration inhibitory factor/tetanus toxoid (**C, F,** and **I**). Ankle joints from interleukin-1 receptor antagonist (IL-1Ra)–knockout 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.)

ECM® 830* In Vivo Electroporation Protocol

Tissue preparation:

Anestitize mice and shave around hind legs, inject anterior tibial muscle with 5mm gap 2-needle array electrodes followed by the injection of the DNA vaccine(25 µg/25 µl 0.9% saline) in between the needles.

Electroporation Settings:

Voltage:		50V
Pulse length:		50 msec
Number of pulses:		3
	repeat 3 pulses with inverted polarity**	
Field Strength:		100 V/cm

* Paper references the BTX T820 generator, which has since been replaced by the ECM 830.

** Polarity is inverted in the ECM 830 by inserting the positive end of the cables into the negative output and the negative end of the cable into the positive output.

Reference;

(1) Onodera, S., Ohshima, S., Tohyama, H., Yasuda K., Nishihira, J., Iwakura, Y., Matsuda, I., Minami, A., and Koyama, Y. 2007. A Novel DNA Vaccine Targeting Macrophage Migration Inhibitory Factor Protects Joins From Inflammation and Destruction in Murine Models of Arthritis. Arthritis and Rheumatism, 56(2): 521-530

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84 October Hill Rd. Holliston, MA 01746 Toll Free Ph: 800-272-2775 or 508-893-8999

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