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Effect of Mizoribine on Effector T Cell-Mediated Immune Responses in Mice

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We examined the effect of Mizoribine (MZR) on various effector T cell-mediated immune responses in mice. MZR prolonged skin graft survival and suppressed a localized graft-versus-host reaction and sheep red blood cell induced DTH. In a collagen induced arthritic mice model, MZR reduced the arthritic index and the swelling of the hind limbs, and suppressed both bone damage and histopathological changes. MZR suppressed the DTH reaction to type II collagen (CII) but had no effect on anti-CII antibody levels in this arthritic model. It is suggested that MZR inhibited these reactions via the inhibition of the effector T cell-mediated immune response. The suppressive effect of MZR on clinical rejection and autoimmune disease might be based on its suppression of the effector T cell-mediated immune response, in addition to humoral immunity.

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Effect of KE-298 on Experimental Arthritis in Mice

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KE-298 is a new immunomodulatory agent with a chemical structure similar to that of D-penicillamine. We compared the effects of KE-298 on type II collagen-induced arthritis (CIA) in mice. At doses of 50 and 100 mg/kg, KE-298 inhibited the severity and development of the collagen-induced arthritis. These inhibitory effects were more pronounced at the dose of 50 mg/kg than at 100 mg/kg. KE-298 inhibited DTH response to type II collagen, but not anti-type II collagen IgG antibody production. Next, we studied the effect of KE-298 on IL-1β and TNF-α production in mice. KE-298 inhibited LPS-induced IL-1β production at doses of 50 and 100 mg/kg. It inhibited TNF-α production at the dose of 50 mg/kg, but not at 100 mg/kg. The results suggest that these effect of KE-298 are closely related to its immunomodulatory action.

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The Effects of Mesoporphyrin on Experimental Arthritis in Mice

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The effects of mesoporphyrin, a novel porphyrin derivative, on type II collagen-induced arthritis (CIA) in mice were studied. Mesoporphyrin (10-30mg/kg) and prednisolone (5mg/kg) reduced the incidence and severity of CIA in mice. Although both agents inhibited type II collagen-induced delayed type hypersensitivity in arthritic mice, only prednisolone inhibited humoral immunity to type II collagen. Staphylococcal enterotoxin B (SEB)-potentiated collagen-induced arthritis and sheep red blood cell-induced delayed type hypersensitivity reaction were clearly inhibited by mesoporphyrin. Moreover, SEB-induced CD-25 expression on T cells was inhibited by mesoporphyrin. These results indicate that mesoporphyrin inhibits CIA by inhibiting the activation of T cells.