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Modulation of collagen-induced arthritis by a natural product resveratrol

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RA is an inflammatory disease with unmet clinical need. Resveratrol, a safe, well-described plant-derived compound, possesses anti-inflammation and immune-regulatory properties in several experimental autoimmune diseases including diabetes, encephalomyelitis (EAE) and colitis. We therefore evaluate the therapeutic effect of resveratrol on collagen-induced arthritis (CIA) and its putative immune modulation in mice.

CIA was induced in DBA1 mice by immunization with collagen II. Different doses of resveratrol were administered before or after the development of CIA. The levels of antibody and cytokines in serum or in draining lymph node (DLN) lymphocyte culture supernatants were measured by ELISA and Th17 cell development in DLN was monitored by flow cytometry.

Either prophyllactic or therapeutic administration of resveratrol attenuated clinical parameters and bone erosion in CIA mice. The arthritis-protective effects were associated with markedly reduced serum levels of pro-inflammatory cytokines and collagen-specific, but not total, IgG, and with reduced numbers of Th17 cells and the production of IL-17 in DLNs. Furthermore, resveratrol was able to inhibit aryl hydrocarbon receptor (AhR) agonist-mediated Th17 cell polarisation in vitro. Thus, resveratrol modulates inflammatory arthritis in rodents by selectively suppressing key cellular and humoral responses necessary for disease development. This may in part explain the protective effects of red wine but importantly may offer a novel, effective and safe pathway whereby novel agents could be developed to treat RA.

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Good response to infliximab in rheumatoid arthritis following failure of interleukin-1 receptor antagonist

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Introduction: To evaluate the efficacy of tumor necrosis factor inhibitor infliximab in patients with rheumatoid arthritis (RA) who were disease resistant to recombinant humaninterleukin-1 receptor antagonist (IL-1Ra).

Methods: A total of 104 patients with active RA despitemethotrexate (MTX) therapy were enrolled. Among them, 27 patients who failed to respond to at least 3-month IL-1Ratreatment ("Switchers")were assigned to an infusion of 3 mg/kg infliximabat weeks 0, 2, 6 and 14, combined with concurrent MTX therapy. The Other 77 patients who had never previously received any biologics were double-blindly randomized in a 2:1 ratio to receive infliximab (n=51, "Naivers")or placebo(n=26, "Controls") plus MTX treatment.Clinical outcomes and safety were assessed at weeks 0, 2, and every 4 weeks thereafter for 18 weeks with the AmericanCollege ofRheumatology (ACR) core set criteria, the Disease ActivityScore in 28 joints (DAS28), and the records of adverseevents (AEs) and abnormal laboratory findings.

Results: At week 18, an ACR20 response was achieved in 56% of Switchersand 61% of Naivers, compared with 23% ofControls (P=0.0013 and 0.0126, respectively).Between the two infliximab-treated groups, Naives had achieved an ACR20 response by week 2, earlier than Switchers; but Switchersachieved a greater benefit from HAQ scorethanNaives. Infliximab was well tolerated, with a similar incidence of AEs, serious AEs and AEs leading to withdrawal across all study groups.However, moreSwitchersdevelopedinfusion-related reactions, compared with the placebo group.

Conclusion: Switching from IL-1Rato infliximab is effective in improving disease activity and maintaining joint function obtained with IL-1Ra.Caution for infusion-related reactions should be required during switching treatment of RA.

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