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Autologous Conditioned Serum

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Introduction

Autologous conditioned serum (ACS) is an autologous blood product enriched in the interleukin-1 receptor antagonist (IL-1Ra), a naturally occurring inhibitor of interleukin- 1 (IL-1). ACS is administered locally to treat conditions in which IL-1 is thought to be an important agent of pathologic conditions. Several reviews have been written on this topic.

IL-1Ra has been produced in Escherichia coli as the recombinant molecule anakinra, marketed as Kineret. Anakinra, in combination with methotrexate, is approved by the US Food and Drug Administration for the treatment of rheumatoid arthritis (RA), self-administered subcutaneously at a daily dose of 100 mg. However, the therapeutic efficacy of anakinra in RA has generally been disappointing, and it is not widely used in this context. Clinical responses in sepsis have also been weak. However, systemic anakinra is effective in systemic juvenile idiopathic arthritis and a variety of rare autoinflammatory disorders; it is also of benefit in gout and pseudogout. There is considerable interest in using anakinra intra-articularly in the treatment of osteoarthritis (OA) and injured joints. An initial, open-label clinical trial in patients with OA of the knee provided highly encouraging results with sustained clinical improvement after intra-articular injection of 100 mg of anakinra. However, a subsequent multicenter, randomized controlled trial (RCT) showed no sustained benefit of intra-articular Anakinra. Nevertheless, there was transient improvement, observed at day 4, in certain parameters, notably pain. The temporary nature of the beneficial effects probably reflects the rapidity with which proteins are removed from joints. An additional clinical trial administered anakinra intra-articularly to patients after rupture of the anterior cruciate ligament (ACL) and again found improvement in certain parameters during the 2-week study period. In a further small, uncontrolled, unblinded study of 6 patients with persistent postsurgical knee effusions, a single 200-mg injection of anakinra decreased pain and swelling, improved range of motion, and permitted return to sporting activities. There is, thus, optimism that IL-1Ra could prove efficacious in injured and arthritic joints if there were a way to maintain therapeutic concentrations intra-articularly. Gene delivery provides one technology for achieving this, and proof of principle

has been established in animal models and human clinical trials for RA. Genetic delivery of IL-1Ra into human knee joints with OA is at an advanced preclinical stage of development.