Biological Therapy in Rheumatic Disorders

Chia-Li Yu, Department of Medicine, National Taiwan University Hospital & National Taiwan University College of Medicine, Taipei, Taiwan

Rheumatic diseases are recognized as a group of chronic, progressive, and immune-mediated inflammatory disorders. Until recently, the treatment options for these disorders have been limited to non-steroid anti-inflammatory drugs (NSAIDs), glucocorticosteroids, disease-modifying anti-rheumatic drugs (DMARDs), and physical therapy. However, these therapies are not efficacious for some patients. Biological agents that target different immune-mediated inflammatory molecules were been designed for potential treatment of these intractable cases. The new therapies include anti-cytokine therapy (TNF-α, IL-1, IL-6, IL-12, IL-15, IL-18, IFN-γ), anti-co-stimulatory molecules (CD_{40}/CD_{40} ligand, CTLA-4/CD_{28}/CD_{80}/CD_{86}), specific antibodies against auto-reactive T and B cells (anti-T cell subsets, anti-CD_{20}), anti-angiogenesis factors, and anti-adhesion molecule therapy (LFA-1, LFA-3, ICAM). Among these new strategies, anti-TNFα therapy (recombinant human soluble p75TNF receptor-IgGFc fusion protein or dimeric/humanized monoclonal antibody) has been proved effective in the treatment of rheumatoid arthritis (RA), psoriasis and psoriatic arthritis (PsA), ankylosing spondylitis (AS), and inflammatory bowel disease. B cell-depleting therapy by anti-CD_{20} monoclonal antibody and different anti-cytokine therapy also showed promising effectiveness in the treatment of refractory SLE. In the early 1990s, gene therapy by intra-articular transfection of anti-inflammatory cytokine genes such as IL-1 receptor antagonist (IL-1Ra) became a novel anti-arthritis strategy. In addition, systemic gene delivery in animal models of RA with different cytokine/ cytokine receptors or other immune-relevant genes to suppress immune-mediated inflammatory reactions were successively reported. Immunoablation followed by autologous hematopoietic stem cell transplant was also explored in patients with severe systemic lupus erythematosus (SLE) who are unresponsive to conventional therapies. New development of DMARDs is also concomitant in progression recently. Inhibitors for purine nucleotide (Mycophenolate mofetil) and pyrimidine nucleotide synthesis (Leflunomide) have been clinically used in the treatment of SLE and RA, respectively. It is conceivable that the coming years promise to an exciting time for the development and trial of new pharmacological and biological agents for rheumatic disorders as we benefit from further understanding their molecular pathogenesis.