REVIEW

GENETICS IN RHEUMATOLOGY
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Summary. Genetic and environmental factors contribute significantly to etiopathogenesis of autoimmune rheumatic diseases. Genes affect enzyme activity and cytokine synthesis, encode receptor activators, etc. The presence of certain genes not only predetermines the occurrence of a disease, its clinical manifestation and mode of progression, but also influences the effect of therapy. This review clarifies basic genetic concepts, related with predisposition to main rheumatic diseases, such as Mendel's laws, penetrance and variable expression, phenocopies and genetic variants.

Key words: genetics, deoxyribonucleic acid, rheumatic diseases

INTRAVERNOS IMMUNOGLOBULIN IN AUTOIMMUNE DISEASES – MECHANISMS OF ACTION
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Summary. Intravenous immunoglobulin (IVIG) is a blood product obtained from the serum of 1,000 to 15,000 healthy donors. It contains immune antibodies and physiologic auto-antibodies. Natural auto-antibodies enable the restoration of impaired immune regulation. The immunomodulatory and anti-inflammatory effects of IVIG are manifested through different mechanisms of action: influence on immune processes via the F(ab′)_2 variable regions; binding of the Fc fragments to a range of Fc receptors; complementary binding within the Fc fragment. IVIG contains a large set of anti-idiotypic antibodies, which bind complementary pathogenic auto-antibodies. IVIG has been demonstrated to inactivate auto-reactive T-cells by competing for and interrupting their interactions with antigen-presenting cells (APC). The balance of cytokines also appears to be restored by the IVIG. The individual mechanisms have different significances in different settings.

Key words: mechanisms of action, intravenous immunoglobulin, autoimmune diseases, immunotherapy

ACTUAL POSSIBILITIES AND PERSPECTIVES OF BIOLOGICAL AGENTS (BAs) IN THE TREATMENT OF SYSTEMIC VASCULITIDES. I. BAs IN SYSTEMIC SMALL VESSEL VASCULITIDES
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Summary. The review presents the hitherto available data on the use of biological agents (BAs) in the treatment of systemic small vessel vasculitides. BAs are applied in recurrent or refractory to conventional therapy vasculitides. Predominantly favourable results in inducing remission are obtained by the TNF-inhibitor infliximab and the anti-CD52 MAB alemtuzumab in ANCA-associated vasculitides (AAV) (Wegener's granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome) and particularly by the anti-CD20 MAB
rituximab in AAV and cryoglobulinemic vasculitis. These results enable reduction or discontinuation of corticosteroid and/or immunosuppressor dosing. Less clarified are their possibilities as a maintenance therapy, particularly in long-term treatments.

**Key words:** biological agents, ANCA-associated vasculitides, cryoglobulinemic vasculitis

THE ROLE OF THERMOGRAPHY IN RHEUMATOLOGICAL PRACTICE
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**Summary.** Thermography is a diagnostic method, which creates “a map of infrared thermal imaging of the human body”. The human body radiates infrared energy; thus, one of the mechanisms of thermoregulation between surface of the body and environment is realized. The body’s infrared radiations can be detected by a thermograph, as in this way a thermogram is obtained. Skin temperature is largely a reflection of the structural state of skin vasculature and the changes in the regulation of vascular tonus. Temperature change is a result of different pathological processes. Thermography is an insufficiently studied method, which can aid diagnosis of different diseases in rheumatological practice, such as rheumatoid arthritis, activated osteoarthritis, Raynaud’s phenomenon, reflex sympathetic dystrophy, scleroderma, soft-tissue rheumatism, fibromyalgia, Paget’s disease. Thermography can be used to monitor the effects of applied local or systemic therapy.

**Key words:** thermography, diagnostic method, therapy

ORIGINAL ARTICLES

ASSOCIATION OF TRANSFORMING GROWTH FACTOR PROMOTER POLYMORPHISM WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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**Summary.** The aim of this study was to evaluate the association of −509C/T promoter polymorphism of TGF-β1 gene with systemic lupus erythematosus (SLE) and clinical features in Bulgarian population. A total of 149 patients with SLE and 134 healthy controls were genotyped for the −509C/T polymorphism of TGF-β1 by restriction fragment length polymorphism (RFLP)–PCR assay. There were no significant differences in allele frequencies of −509C>T polymorphism of TGF-β1 gene between the SLE patients and healthy controls. However, the frequency of heterozygous genotype among the SLE patients (53%) was higher compared to healthy controls (42%) with borderline significance and OR = 1.52; 95% CI, 0.96–2.59, P = 0.059. In addition, heterozygous
genotype was significantly higher in the SLE patients with haematological disorders (60%) compared to patients without these clinical features (38%) with OR = 2.41; 95%CI: 1.1-5.32; p = 0.016. The heterozygous genotype was also found to be slightly associated with anti-DNA positivity (OR = 2.0; 95%CI: 0.96-4.2; p = 0.045). In conclusion, our results suggest that -509C > T polymorphism of TGFβ1 may play a role in the susceptibility to SLE in the Bulgarian population. Also, TGF-β1 polymorphism was related to specific clinical manifestations of the disease pointing TGFβ1 polymorphism as one of the genetic factors that explain the heterogeneity seen in/with SLE.

Key words: gene polymorphism, SLE, TGF-β1
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