

AUTOROME

Rare Autoimmune diseases, such as scleroderma, systemic lupus erythematosus, antiphospholipid syndrome, systemic vasculitis and autoimmune lymphoproliferative syndrome, are severe, chronic conditions causing substantial morbidity and sometimes leading to mortality in affected persons, especially children and the elderly.

AUTOROME, a three-year European Commission FP6 project (contract LSHM-CT-2004-005264) receiving €2.7 million in funding, is headquartered in Rostock, Germany under the leadership of Professor Hans-Jürgen Thiesen, director of the university's Institute for Immunology. AUTOROME has a network of 12 research groups from centres of excellence in five European countries and Israel.

“From immune responses in rare autoimmune diseases to novel therapeutic intervention strategies - a personalized medicine approach” states the AUTOROME website, reflecting the aim of the project to research new diagnostic methods and achieve an improved understanding of autoimmune processes in patients.

Four work packages have been defined to meet these goals: I. Antigen / Autoantibody Mapping, II. Idiotype-specific Peptides, III. Dysfunction of the Immune System, and IV. Basic Developmental Mechanisms in the Immune System

AUTOROME seeks to achieve its objectives by profiling autoantigens and autoantibodies to determine the major autoreactive epitopes, by addressing mechanisms that determine the initiation, progression and chronicity of the humoral immune response on the cellular level (T-cells, APC cells, B-cells, epithelial cells), by characterizing cellular differentiation, maturation and migration processes with a strong focus on B cell development, making use of animal models, and by developing therapeutic approaches to eliminate autoantibody producing cells.

Diagnostic tools assessing the relevance and distribution of pathogenic antibodies in individual patients are one essential milestone in generating and selecting appropriate therapeutic intervention strategies. Hereto, diagnostic kits as well as autoantigen and antibody chips will be developed and validated in clinical settings. Knowledge derived from this analysis will be instrumental to improve the disease monitoring of patients suffering from severe autoantibody-mediated autoimmune diseases. The deliverables of the AUTOROME project will lead to a better understanding of the interplay and contribution of humoral and cellular immune mechanisms. Finally, this enterprise might pave the way to more personalized therapeutic and prevention strategies.

Reducing the incidence, prevalence and severity of autoimmune diseases in turn diminishes both the social and economic impact of this group of illnesses for the patient and the society at large.

To date, all four work packages have reached the milestones outlined in the technical annex. In short, protocols have been exchanged and standardised between the groups participating in the individual work packages. A common reporting platform has been established using the intranet of the URL www.autorome.org to report the progress of the individual projects.

Clinical samples as well as the corresponding documentation were continuously collected. Pilot studies were initiated using peptide and protein chips. Novel autoantigens were immunoprecipitated and the nature of these proteins is currently being determined by mass spectrometric analysis. B and T cell receptor repertoires of patients suffering from Autoimmune Lymphoproliferative Syndrome (ALPS) were determined. RNA expressions are studied on cell subsets derived from sorted PBLs of patients suffering from scleroderma. Si RNA approaches are currently tested in cell culture systems to interfere with autoantibody production. Animal models, in vitro and cell culture systems are used to study the molecular nature of these disease processes in greater depth.

Expert knowledge present in various disciplines from experimental and clinical medicine in Europe and Israel have been combined to tackle molecular and cellular mechanisms that play a role in the pathologies of rare autoimmune diseases. Technologies applied in functional genomics and basic immunology as well as cellular in vitro and animal models have been integrated in a combined interdisciplinary research effort to study the etiology and progression of rare autoimmune diseases. Finally, this undertaking should 1) elucidate whether and how genetic and environmental factors come together leading to the diseases under study, and 2) should lead to novel diagnostic and therapeutic tools that take into account the nature of the disease the individual suffers from. The academia would love to understand how the interplay of cellular and humoral components of the immune system leads to diseases as seen in the AUTOROME project.

Visit the AUTOROME website:

www.autorome.org