ADVANCES IN MOLECULAR AND CLINICAL RHEUMATOLOGY

Scientific symposium on the occasion of the 80th anniversary of the Hungarian Association of Rheumatologists

Budapest, September 17–18, 2008

PROGRAMME AND ABSTRACTS

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Institute of Musicology, Castle Buda

Welcome

Dear Guests and Colleagues,

You are most cordially welcome to the international scientific symposium "Advances in Molecular and Clinical Rheumatology".

This meeting has been organized on the occasion of the 80th anniversary of the Hungarian Association of Rheumatologists (HAR). Indeed, the Association was established in 1928 so it can be regarded as one of the most traditional rheumatology societies in Europe. During its 80 years of activity the HAR has always carried out its aims defined at the foundation, i.e. served the improvement of patients with rheumatic diseases, the interest of specialists and the advance of science. In fact, rheumatic disorders have a major and increasing impact on the quality of life of our patients and the financial burden is a considerable determinant of healthcare budgets. Many efforts have been made against these conditions worldwide and in Hungary especially in the current "Bone and Joint Decade".

The scientific programme of the symposium will be covering the hot topics of molecular and clinical rheumatology therefore opinion leaders from different parts of Europe, overseas, Middle-East and from Hungary have been invited to deliver exciting state of the art lectures. Thanks for their contribution to make this anniversary a real feast. Attendees represent the top of rheumatologists from home and from beyond the frontiers.

The jubilee event is also to draw attention to the Hungarian scientific community engaged in higher education and research in the field of rheumatology and related areas. Thus the meeting is co-organized by the Hungarian Academy of Sciences and the Semmelweis University, Budapest.

The organizers have spared no effort to ensure that this meeting will be a memorable experience and celebration for all of you. Many thanks the major sponsors for supporting our aims and activity. We wish you to have a nice and useful time in Budapest and here in the Institute of Musicology, in the house of the rich and diverse Hungarian cultural heritage.

On behalf of the Board and the organizers
with best personal regards

Budapest, September 17, 2008.

Prof. Dr. Gyula Poór
Chairman of the symposium
President, HAR

General information

Organizer: Hungarian Association of Rheumatologists

Co-organizer: Hungarian Academy of Sciences; Semmelweis University, Budapest

Chairman of the symposium:
Prof. Dr. Gyula Poór, president of the HAR

Scientific committee:
Gyula Poór (Budapest), László Czirják (Pécs), András Falus (Budapest), Pál Géher (Budapest), Peter Gergely jr. (Budapest), Tibor Glant (Chicago, USA), Gábor Illei (Bethesda, USA), Emese Kiss (Budapest) Tore K. Kvien (Oslo, Norway) Péter Lakatos (Budapest) Burkhard Leeb (Stockerau, Austria), Wlodzimierz Maslinski (Warsaw, Poland), Karel Pavelka (Prague, Czech Republic), Andras Perl (Syracuse, USA), José Antonio P. da Silva (Coimbra, Portugal), Yehuda Shoenfeld (Tel-Hashomer, Israel), Zoltán Szekanecz (Debrecen), Anthony D. Woolf (Truro, UK)

Organizing committee:
Gyula Poór, György Hittner, Csilla Várszegi, and the Board of the Association

Organizing office:
Dekantil Ltd. (Budapest, Országház u. 2,
tel/fax: 36 1 213-6222, 36 1 214-3814, email: dekantil@t-online.hu)

Venue of the symposium:
Institute of Musicology (1014 Budapest, Táncsics M. u. 7,
tel: 36 1 214-6770, fax: 36 1 375-9282 e-mail: info@zti.hu)

Accomodation for the faculty:
Hunguest Europa Hotels & Congress Center (1021 Budapest, Pálos utca 2., Tel.: 36 1 391-5100, 36 1 391-5153, Fax: 36 1 391-5171, www.hunguesthotels.hu, www.europacongress.hu)

Note: The costs of the symposium are covered by the Hungarian Association of Rheumatologists so it's free for the invited participants, including registration, lunch and refreshments. However, accommodation and insurances are not provided for the attendees during the meeting. The organizers cannot be held responsible in case of loss, theft or damage of any personal things. The organizers kindly ask all participants not to use mobile phones in the lecture hall.

Scientific programme

● ***September 17.***

9.30–10.00 **Welcome addresses**

Gyula Poór: President, Hungarian Association of Rheumatologists
József Pálinkás: President, Hungarian Academy of Sciences
István Karádi: Dean, Semmelweis University, Budapest
José António P. da Silva: President, European Board of Rheumatology (UEMS)
László Czirják: Secretary General, EULAR

10.00–11.00 **Opening lectures**
Chairmen: László Czirják, Pál Géher

Tore K. Kvien (Past President, EULAR, Oslo): Principles of research, management and education in rheumatology
Gyula Poór (Budapest, Hungary): The activity of the Hungarian Association of Rheumatologists, selections from the history of medicine in Hungary

Discussion

11.00–11.20 Coffee break

11.20–12.30 **General pathophysiology in rheumatology**
Chairmen: Tibor Glant and Andras Perl

András Falus (Budapest, Hungary): Wide-scale genomic analysis of inflammation – lessons for rheumatology
Yehuda Shoenfeld (Tel Hashomer, Israel): The mosaic of autoimmunity — the role of infection
Zoltán Szekanecz (Debrecen, Hungary): Adhesion and angiogenesis in inflammatory rheumatic diseases

Discussion

12.30–14.00 Lunch

14.00–15.10 **Specific pathogenesis of autoimmune disorders**
Chairmen: Gabor Illei and Yehuda Shoenfeld

Andras Perl (Syracuse NY, United States): Metabolic checkpoints of T-cell activation and death pathway selection – Biomarkers and targets for treatment in systemic lupus erythematosus
Wlodzimierz Maslinski (Warsaw, Poland): The role of bone marrow in the pathogenesis of rheumatoid arthritis
Peter Gergely jr. (Budapest, Hungary): Pathophysiological and clinical significance of autoantibodies against citrullinated proteins

Discussion

15.10–15.30 Coffee break

15.30–17.00 **New approaches in metabolic bone diseases**
Chairmen: Burkhard Leeb and Wlodzimierz Maslinski

Tibor Glant (Chicago, United States): Cytokine-controlled RANKL and OPG by synovial fibroblasts – Fibroblast-mediated pathological bone resorption
Anthony D. Woolf (Truro, United Kingdom): Recent pathogenetic and therapeutic aspects of osteoporosis
Gyula Poór (Budapest, Hungary): Pathogenesis and management of Paget's disease of bone
Péter Lakatos (Budapest, Hungary): Laboratory markers in metabolic bone diseases

Discussion

17.00– **Concert**

September 18

9.00–10.10 **Novel therapies in inflammatory rheumatic diseases**
Chairmen: Karel Pavelka and Anthony D. Woolf

José António P. da Silva (Coimbra, Portugal): Present and future biological therapy in rheumatoid arthritis
Gabor Illei (Bethesda, United States): Experience with experimental biological treatment and local gene therapy in Sjögren's syndrome
Emese Kiss (Budapest, Hungary): Therapeutic targets in SLE

Discussion

10.10–10.30 Coffee break

10.30–12.00 **Novel therapies in inflammatory rheumatic diseases (cont.)**
Chairmen: José António P. da Silva and Gyula Poór

László Czirják (Pécs, Hungary): Outcome measures and treatment options in systemic sclerosis
Burkhard Leeb (Stockerau, Austria): Biological agents in spondylarthropathies
Karel Pavelka (Prague, Czech Republic): Importance of biological registries
Pál Géher (Budapest, Hungary): New approaches of glucocorticoid and NSAID therapy in inflammation

Discussion

12.00 Handover of honorary membership's diploma
Closing of the symposium

12.15–13.15 Lunch

Abstracts

Abstracts are listed in the order of the lectures presented

- **Principles of research, management and education in rheumatology**

Tore K. Kvien
Past President, EULAR;
Diakonhjemmet Hospital and University, Oslo, Norway

Research in Europe has developed over the last years. EULAR wants to be an active player in fostering research and education. New knowledge is disseminated through educational activities including online course, dedicated courses in special areas, and post-graduate course.
Another important aspect is elaboration or recommendations of management which also supports standardization of management across countries.
EULAR is also working to raise arise the awareness of rheumatic diseases in EU. Rheumatic diseases are now included a specific topic among chronic diseases in research framework program 7 and two big multinational rheumatological research projects have been funded from EU over the last three years. Additionally, the project "European Musculoskeletal Conditions. Surveillance and Information Network" was recently approved and funded by the second programme of Community Action in the field of Health.
Several opportunities exist on the national level to foster research. My own experience from Oslo is based on foundation of several clinical/epidemiological research databases. Cohorts of patients have been followed for up to 15 years and registers — both disease and treatment based — are important tools for data collection. Epidemiological data are important when arguments are presented about the organization of care models for rheumatic diseases. Databases and cohort studies can also be used for translational research. Robust clinical data and outcomes are important when biomarkers or immunological findings are linked to clinical information.
In conclusion, improved opportunities are available on a national and European level, both for research and education in rheumatic diseases.

- **The activity of the Hungarian Association of Rheumatologists, selections from the history of medicine in Hungary**

Gyula Poór
National Institute of Rheumatology and Physiotherapy;
Semmelweis University, Budapest

Recognizing the social impact of rheumatic diseases, the Hungarian Physicians' Rheumatism Association (HPRA) was established in 1928. The Association was among the first ones to join ILAR in the year of its establishment which led to the international organisation's first world congress being held in Budapest. After the war the HPRA was dissolved and its functions were taken over by the Special Group for Rheumatism, organized by the trade unions.

Its legal successor, the Hungarian Associaton of Rheumatologists (HAR) was established in 1966 and it significantly contributed to the realization of modern rheumatology in Hungary. In 1991 Budapest was the venue of the EULAR congress. The HAR organizes national and international meetings, publishes scientific and informational journals, has a foundation and a patients' association, as well as territorial and professional sections and a youth forum are operated.
The Association during its 80 years of activity has always carried out its aims defined at its foundation, i.e. served the improvement of patients with rheumatic diseases, the interest of specialists and the advances of science.

- **Wide-scale genomic analysis of inflammation – lessons for rheumatology**

András Falus
Department of Genetics, Cell- and Immunobiology, Semmelweis University, Budapest, Hungary

Genomics, i.e. genome-based biology, a recent synthesis of genomicdatabases, high-throughput nano-biotechnologies, bioinformatics and computer science provides an entirely new, complex concept for basic and medical sciences. The recent leading tendency based on multicentric grid-like studies designates understanding of genetic networks behind the complex biological pathways in health and disease, including acute and chronic inflammation. For the revolutionary development of preventive, diagnostic and therapeutic medical research integrative genomics assigns new approaches through *systems biology*. These trends are well exemplified by unique hits in immungenomics, pharmacogenomics, human biology and evolution. Major new trends, perspectives, ethical issues as well as potential risks are to be shown in the review with particular attention to chronic inflammation and rheumatological diseases.
Innovative technologies such as detection of gene expression pattern (mRNA microrray), microRNA pattern, large scale determination of single mucleotide polymorphism (SNP), application of si (silencing) RNA, peptide arrays, peptides libraries are opening new vistas for epitope identification. A next generation of high throughput systems will probably make peptides available also with all the potential post-translational modifications (e.g. arrays of glycopeptides). Advanced bioinformatic technologies, such as gene pathway analysis and Bayes statistics will open entirely new perspectives in medical biology, including inflammation and rheumatology.

- **The mosaic of autoimmunity — the role of infection**

Yehuda Shoenfeld
Department of Medicine 'B' & Center for Autoimmune Diseases, Sheba Medical Center, Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases, Sackler Faculty of Medicine, Tel-Aviv University Tel Hashomer, Israel

The etiology of autoimmune diseases is multi-factorial, consisting of immune defects, genetics, hormonal and environmental factors playing in concert. Almost each infectious agent has been named as inducing a variety of autoantibodies, and in some circumstances leading to an overt disease.

EBV, CMV, H. Pylori, Parvo virus, B-19 consist a case in point. Each specific autoimmune disease may be caused by different bacteria and/or viruses. Many mechanisms by which an infectious agent can cause autoimmunity have been listed in the literature, with molecular mimicry being singled out. Examples entail streptococci, rheumatic fever, Guillain- Barre syndrome and many bacteria. We shall hence delineate the infectious origin of the newly described anti-phospholipid syndrome.
If indeed infectious agents are implicated in the etiology, it will be surprising if vaccines would not be involved in autoimmunity. This is even more emphatic when bearing in mind the adjuvant effects of vaccines, and especially multiple vaccines (i.e. MMR).
The literature is indeed flooded with case reports alluding to diverse vaccines followed by the emergence of a variety of autoimmune diseases. Some experimental models in mice and dogs support this assumption. Yet, the vaccine — autoimmunity cause and effect relationship is still debatable. The latter is fueled by the large epidemiological negative result studies.
It seems that parallel to the infectious — autoimmunity relationship, the vaccine — autoimmunity relationship is also conditioned by the ingredients (antigens) incorporated in the individual vaccine; its adjuvanicity, and above all by the genetic background of the individual.

- **Adhesion and angiogenesis in inflammatory rheumatic diseases**
  Zoltán Szekanecz
  University of Debrecen Medical Center, Institute of Medicine, Department of Rheumatology, Debrecen, Hungary

A number of cell adhesion molecules (CAMs) including selectins and integrins are involved in leukocyte recruitment uncderlying the pathogenesis of inflammatory synovitis. These CAMs interact with soluble inflammatory mediators, such as cytokines and chemokines. The presence of various CAM pairs and the existence of distinct steps of rolling, activation, adhesion and migration account for the diversity and specificity of leukocyte-endothelial interactions. Chemokines and their receptors drive inflammatory leukocytes into the synovium. Leukocyte ingress into the synovium is further perpetuated by angiogenesis, the formation of capillaries from pre-existing vessels. A number of soluble and cell-bound factors may stimulate or inhibit angiogenesis. The outcome of inflammatory and other "angiogenic diseases", such as various forms of arthritis, depends on the imbalance between angiogenic and angiostatic mediators. Some CAMs and chemokines are also involved in neovascularization. There have been several attempts to therapeutically interfere with the cellular and molecular mechanisms described above. Specific targeting of leukocyte adhesion, CAMs, chemokines, chemokine receptors and/or angiogenesis, primarily by using agents with multiple actions, may be useful for the future management of arthritis.

- **Metabolic checkpoints of T-cell activation and death pathway selection – Biomarkers and targets for treatment in systemic lupus erythematosus**
  Andras Perl
  SUNY College of Medicine, Syracuse NY, United States

The cause of systemic lupus erythematosus (SLE) is unknown and current therapies have limited efficacy. A rational therapeutic approach requires biomarkers relevant for disease pathogenesis and fluctuation of disease activity. The mitochondria play crucial roles in T-cell activation and death; however, their role in altered lymphocyte activation and death is unknown in SLE. Importantly, lupus T-cells exhibit mitochondrial hyperpolarization (MHP) and consequential ATP depletion, resulting in decreased activation-induced apoptosis and predisposition to necrosis, which stimulate inflammation in SLE. The mammalian target of rapamycin (mTOR) is a large protein kinase that is associated with the outer mitochondrial membrane and senses changes in the transmembrane potential of T-cells. Focusing on mitochondrial dysfunction, we utilized rapamycin for treatment of patients resistant or intolerant to conventional medications. Oral rapamycin markedly reduced disease activity and prednisone use. In rapamycin-treated patients, MHP persisted while mTOR activity and CD3/CD28-induced Ca2+ flux were normalized, indicating that 1) mTOR is a sensor and effector of MHP and 2) increased Ca2+ fluxing is downstream of MHP in lupus T-cells. Thus, MHP, mTOR activation, and enhanced Ca2+ fluxing are biomarkers of T-cell dysfunction and disease activity in patients with SLE.

- **The role of bone marrow in the pathogenesis of rheumatoid arthritis**
  Wlodzimierz Maslinski
  Department of Pathophysiology and Immunology, Institute of Rheumatology Spartanska, Warsaw, Poland

Despite intensive research and great progress in understanding mechanisms contributing to chronic inflammation and joint destruction in rheumatoid arthritis (RA), the pathogenesis of this disease still remains unknown. Recent data indicate that beside affected joints, lymphoid organs, especially the bone marrow (BM) may actively participate in the initiation and perpetuation of the autoimmune-inflammatory processes in RA. BM edema reflecting true inflammation is often seen both in early as well as in advanced RA. Comparison of RA and osteoarthritis (OA) clearly show overproduction of proinflammatory cytokines IL-1, IL-6, TNF-α, IL-15 and IL-17, and osteoclastogenic RANKL in RA bone marrow. Moreover, activated, memory type of CD4+ and CD8+, and Th17 T-cells are present in situ. Although at present it is not entirely clear what triggers the inflammation in RA BM, our preliminary data indicate higher frequency and levels of eubacterial DNA than in OA BM. Functional TLR9, responding to bacterial DNA by increased proinflammatory cytokine production (TNF-α, IL-6), overexpression of costimulatory molecules (CD86), proliferation and differentiation toward plasma cells, are gained by BM B-cells at pre-B/immature B-cell stages of their maturation in BM. Freshly isolated RA BM CD20+ B-cells exert higher CD86 expression suggesting their activation in situ. Taken together these data indicate the role of BM compartment in the initiation and/or propagation of inflammation in RA that should be considered for successful targets in RA.

- **Pathophysiological and clinical significance of autoantibodies against citrullinated proteins**
  Peter Gergely jr.
  National Institute of Rheumatology and Physiotherapy; Semmelweis University, Budapest, Hungary

Novel data suggest that citrullination has a key role in the formation of autoantigens in rheumatoid arthritis (RA). Citrullination includes the posttranslational transformation (deimination) of arginyl residues of certain proteins into citrullyl residues by the peptidylarginine deiminase enzymes. Antibodies to citrullinated proteins (ACPAs) are highly specific serological markers for RA often found early in the disease course and are associated with more severe joint destruction and disease activity. Furthermore, ACPAs have evolved from being mainly a diagnostic or prognostic marker to being recognized as a system that contributes significantly to fundamental etiologic and pathogenetic features of RA. Based on the presence or absence of such antibodies, rheumatoid arthritis can be divided into two distinct clinical subsets each of those having a different genetic background. Moreover, the production of ACPAs may also be influenced by environmental factors such as tobacco smoking. This review summarizes novel findings regarding the diagnostic and pathophysiological role of ACPAs in rheumatoid arthritis.

- **Cytokine-controlled RANKL and OPG by synovial fibroblasts – Fibroblast-mediated pathological bone resorption**
  Tibor Glant
  Section of Molecular Medicine, Departments of Orthopedic Surgery, Biochemistry, Internal Medicine (Section of Rheumatology) and Immunology/Microbiology, Rush University Medical Center, Chicago, USA

The goal of this study was to determine whether pro-inflammatory cytokine treatment or the complete absence of select cytokines modulates the expression of receptor activator of NF-κB ligand (RANKL) and osteoprotegerin (OPG) in synovial fibroblasts.
Fibroblasts were isolated from normal and rheumatoid human synovium, and from normal or arthritic joints of wild-type and cytokine gene-deficient (IL-4$^{-/-}$ and IFN-γ$^{-/-}$) mice. Fibroblasts were stimulated with pro-inflammatory (TNF-α, IL-1β and IL-17) or anti-osteoclastogenic (IL-4 and IFN-γ) cytokines alone or in combination, and the expression of RANKL and OPG was measured.
Pro-inflammatory cytokine-stimulated fibroblasts from rheumatoid and arthritic mouse joints expressed higher levels of RANKL and OPG than those from normal joints. IL-4 suppressed RANKL and increased OPG expression, IFN-γ reduced the production of both, while IL-17 had only a modest effect on RANKL or OPG expression. Additive effects in combination treatments (TNF-α/IL-17 or IL-1β/IL-17) were found only in the human system. Extensive joint destruction was observed in the arthritic joints of IL-4-deficient mice, along with a corresponding upward shift of RANKL/OPG ratios. However, IL-17 deficiency did not attenuate arthritis or reduce bone resorption.

Pro-inflammatory cytokines induce expression of RANKL and OPG in both human and murine synovial fibroblasts. RANKL/OPG ratios are shifted in favor of bone protection by IL-4, and, to a lesser extent, IFN-ã treatment. Unexpectedly, IL-17-deficiency alone does not induce reduced inflammatory bone destruction. Our results suggest that synovial fibroblasts may significantly contribute to bone resorption through modulation of RANKL and OPG production in a cytokine-rich milieu of inflamed joints.

- **Recent pathogenetic and therapeutic aspects of osteoporosis**
  Anthony D. Woolf
  Rheumatology, Institute of Health Care Research, Peninsula College of Medicine and Dentistry, Universities of Exeter and Plymouth; Duchess of Cornwall Centre for Osteoporosis Royal Cornwall Hospital Truro, United Kingdom

Osteoporosis is a major cause of fractures in all populations. It is characterised by reduced bone mass and loss of microarchitecture, which is universally associated with aging. In addition there are other recognised risk factors and specific causes of osteoporosis including genetic, physiological, pathological and environmental factors. An increased understanding of bone biology is leading to advances in therapies and an increased understanding of risk factors is improving targeting therapy at those who will most benefit. Improving lifestyle by ensuring adequate calcium, vitamin D and physical activity with avoidance of low BMI, smoking and excess alcohol will overall improve bone health of the population but more effective interventions are needed for those at highest risk or with osteoporosis. These have predominantly been anti-resorptives but now there are agents that stimulate bone formation. Fracture prevention has been demonstrated but there remains the challenge as to how to target those most at risk and ensure adherence to gain full benefit. These issues and the latest evidence will be discussed.

- **Pathogenesis and management of Paget's diasease of bone**
  Gyula Poór
  National Institute of Rheumatology and Physiotherapy; Semmelweis University, Budapest

Paget's disease of bone (PDB) is characterized by focal regions of highly exaggerated and disorganized bone remodeling, with abnormalities in all phases of the remodeling process. The disease can affect one or several bones throughout the skeletal and can be associated with bone pain and other complications, such as bone deformity pathological fractures, osteoarthritis, deafness or nerve compression syndromes.
Genetic factors play an important role in PDB and several mutations have been identified that may lead to familial Paget's disease. These include SQSTM1 which encodes p62, TNFRSF11A which encodes RANK, TNFRSF11B which encodes osteoprotegerin and VCP which encodes p97. All of these genes are critical in the RANK-NFκB signalling pathway and it is likely that mutations predispose to PDB by disrupting normal signalling leading to osteoclast activation. Our research group demonstrated significant overexpression of the genes of the interferon signalling pathway that may play central role in the aberrant osteoclastogenesis. Environmental factors also

contribute to PDB. Most research has focused on paramyxovirus infection but evidence in favour of the involvement of viruses in PDB remains conflicting.
Management of PDB is based on giving inhibitors of osteoclastic bone resorption and bisphosphonates are the treatment of first choice. Bisphosphonate therapy is highly effective at reducing bone turnover and at controlling pain. Supportive treatments and orthopaedic surgery are also required for the management of patients with Paget's disease.

- **Laboratory markers in metabolic bone diseases**
  Péter Lakatos
  1st Department of Medicine, Semmelweis University Budapest, Hungary

Laboratory markers of metabolic bone diseases have become part of the everyday clinical evaluation of these disorders. In the work-up of primary and secondary *osteoporosis*, routine chemistry provides basic information in terms of the underlying pathogenetic processes. Hormone determinations are also inevitable part of the diagnostic procedure. Specific bone biochemical markers, such as collagen crosslinks, tartarate-resistant acid phospohatase, etc, proved to be a useful tool in fracture risk prediction and monitoring of therapy. In *osteomalacia*, direct measurement of serum 25-hydroxy-vitamin D_3 levels assures correct diagnosis. Recognition of primary and secondary *hyperparathyroidism, renal osteodystrophy and Paget's disease* of bone has been made possible by a combination of routine, hormonal and specific markers. The determination of new compounds contributes to the diagnosis of *metastatic bone* diseases as well as the assessment of *cartilage* deterioration. Recently, genetic markers including COL1A1 sp1 and osteoprotegerin Lys3Asn polymorphisms start to be utilized in the management of metabolic bone disorders. In the near future, high-throughput micro- and macroarray expression and polymorphism analyses may enable us to identify subgroups within these disorders and provide more personalized treatment modalities for our patients.

- **Present and future biological therapy in rheumatoid arthritis**
  José António P. da Silva
  President, European Board of Rheumatology (UEMS);
  Reumatologia Hospitais da Universidade Coimbra, Portugal

The development of biological therapies represented a true revolution in the treatment of rheumatoid arthritis, leading to remarkable improvements in the control of disease activity, structural destruction and especially quality of life. Despite the limitations imposed by cost, growing numbers of patients are exposed to these therapies at earlier stages of the disease. Toxicity has proved to be manageable. Nevertheless, a significant proportion of patients still do not show satisfactory response to the available biological therapies. This illustrates the complex variability of the biological processes underlying the disease and feeds the need for progress.
The immediate future will probably be dominated by changes in strategy, especially at the level of medical practice. The productivity of this approach has been shown by important innovative studies such as the BeSt, the TICORA and CAMERA, among others. Equally interesting to follow will be investigations regarding the optimized contribution of bisphosphonates and glucocorticoids. The role of available biologicals besides anti-TNF, such as anti-IL-1, anti-CD20, anti-CTLA-4, anti-IL6 and anti-RANKL, as well as their combinations will be clarified, hopefully in ways that lead to more individually tailored therapies.
Such developments will require not only new trials, careful analysis of extensive practice registries but also a refreshed statistical approach that recognizes and explores the individual variability, while keeping the "dictatorship of the mean" under control.
It is far more difficult to foresee the potential contribution of the many new targets under investigation. Rheumatoid arthritis is exceedingly complex and leaves little room for hopes that a single magic bullet will be found to suit all in the future. Promising new targets under exploration include cellular targets e.g. new CD20 targeting antibodies, cytokine targets including lymphotoxin, IL-12/23, IL-17, IL-6, and in, earlier phases, also IL-18 and IL-15. Targeting BLyS and APRIL also looks interesting for reducing B-cell activation in RA.
The complexity of intermediated pathways requires an especially optimistic soul to hope that inhibiting kynases may prove productive in RA. However, research towards disease modification through small molecule inhibitors that target JAK and STAT, syk kinase and p38 and other MAPKs is under way.

- **Experience with experimental biological treatment and local gene therapy in Sjögren's syndrome**
  Gabor Illei
  National Institutes of Health, Bethesda, United States

Biologic therapies have fundamentally changed the treatment of many rheumatologic diseases and have shown that blocking key players in the pathogenesis may translate into significant clinical benefits. However, early attempts with biologics in Sjögren's Syndrome (SS) have been disappointing. Clinical trials with two TNF inhibitors were negative as was a large study with low dose interferon-alpha. Pilot studies with B-cell depleting agents showed modest benefit in improving systemic manifestations with little or no effect on exocrine function. Currently the focus is on key molecules of the inflammatory cascade targeting B lymphocytes, cytokines (BAFF, interferon-alpha) and adhesion molecules (LFA-1). Better understanding of the interaction of inflammation and exocrine dysfunction will identify the ideal targets and for biologic therapy in SS. Even after such a target is identified, the potential toxicities or cost of systemic therapy may not be justified for many patients with SS. An alternative to systemic therapy is local gene therapy. Animal studies have shown that genes delivered by adeno-associated virus vectors to the salivary glands can lead to improvement of inflammation and dysfunction safely without any systemic side effects.

Therapeutic targets in SLE

Emese Kiss
National Institute of Rheumatology, Budapest, Hungary

Lupus is a multifactorial autoimmune disease. Although the survival for SLE patients has increased, there are non-responder cases leading significantly higher mortality in lupus than in the general population. It requires more effective targeted therapies. The pathogenesis of lupus involves all elements of the immune system. Pathogenic autoantibody production and consequent tissue damage is a hallmark of the disease. B-cells are stimulated by autoreactive T-cells that respond to the activation by antigen presenting cells. These processes are mediated by direct cell-cell interactions through cell surface molecules or by cytokines. The clearing of autoantibodies and cell debris is also pathologic. The interruption of co-stimulatory molecules, including CD40-CD40L, CD28-B7, with monoclonal antibodies is a promising therapeutic possibility as well as blocking or depleting B-cells with anti-CD20, -CD22 MoAbs, B lymphocyte stimulator antagonists or B-cell tolerogens.. Abrogation of the type I interferon pathway has also been targeted. The blocking of interleukin-10 may also reduce antibody production. Peptides from pathogenic autoantibodies may be useful in generating anti-idiotypic responses. Besides, high-dose intravenous immunoglobulin therapy may modulate different Fc-gamma receptors. Autologous stem cell transplantation is supposed to have benefitial immune modulating effects further to the used immunoablating chemotherapy. Many other elements of the immune system can surve as a potential target for novel innovative drugs. Clinical trials should find the effective and safe compunds to be introduced into daily practice.

Outcome measures and treatment options in systemic sclerosis

László Czirják
Secretary General, EULAR;
Department of Immunology and Rheumatology, Medical School, University of Pécs, Hungary

Systemic sclerosis (SSc) is characterised by arterial and microvascular lesions, fibrosis, degenerative and inflammatory changes affecting the skin and several internal organs. Our survival analysis of 366 patients with systemic sclerosis (SSc) by Kaplan-Meier univariate analysis showed that renal, cardiac involvement, pigmentation disturbances, malabsorption, a forced vital capacity < 50%, diffuse scleroderma, presence of early malignancy, anaemia, and increased ESR were signs of unfavourable prognosis, whereas anti-centromere antibodies were indicators of a good survival. In the multivariate Cox proportional hazards model the presence of diffuse scleroderma, renal involvement, coexistence of a malignant disease, and increased ESR were bad independent prognostic signs. Elderly age at the onset of disease also caused an unfavourable outcome.
86 SSc-related deaths were recorded during the follow-up. 65% of the deaths were attributed to cardiorespiratory manifestation of disease. Tumour associated early death was found in 12 cases (14%). Our conclusions is that in addition to the well-known factors influencing the outcome (diffuse subset, internal organ involvements, and inflammatory signs), the coexistence of scleroderma with a malignancy also causes a poor outcome.
There is no disease modifying drug therapy of proven efficacy in SSc. The aim of the therapy includes the influence on vascular abnormalities, the fibrosis of the skin and internal organs. In spite of the lack of disease-modifying agents, individualized, well designed therapy can be remarkably efficient in terms of improving the prognosis and quality of life of patients.

Biological agents in spondylarthropathies

Burkhard Leeb
1st and 2nd Dept. of Medicine, State Hospital Stockerau; Lower Austrian Center for Rheumatology; Karl Landsteiner Institute for Clinical Rheumatology Stockerau, Austria

The application of TNF blocking agents proved to be a major step forward in the treatment of seronegative spondylarthropathies, particularly Psoriatic arthritis (PsA) and Ankylosing Spondylitis (AS). However, the number of patients at a need for these drugs is reasonably smaller than in Rheumatoid Arthritis. There is impressive and comparable evidence for all three currently available drugs, namley infliximab (IFX), etanercept (ETA) and Adalimumab (ADA).
TNF-alpha inhibitors for PsA and AS patients are recommeded in both, DMARD-resistant polyarticular synovitis and in pelvispondylitic disease not responding to Nonsteroidals, as there is no evidence to supprt the use of DMARDs in patients with exclusively axial disease. TNF-alpha inhibitors have demonstrated impressively their benefit in reducing AS activity. With respect to anterior uveitis in AS patients treatment with both antibodies turned out to be efficacious in contrast to the receptor construct.
IFX, ETA as well as ADA also proved their efficacy for the treatment of PsA in controlled trials. Concomitant MTX therapy is still in discussion, not only for greater efficacy but also to diminish the risk of developing neutralizinig antibodies. In the ADEPT study, however, MTX did not appear to be decisive for the the 48 week efficacy of ADA.. In addition to antiarthritic efficacy ETA, IFX and ADA cause rapid improvement of skin and nail lesions in a reasonable number of patients.
Whereas all TNF-blockers are cliniically impressively effective in AS and PsA patients, there capability of slowing down spinal radiographic progression in AS turned out to be less than expected. With the exception of anterior uveitis, the TNF-blockers provide identical chances for response on the group level.

Importance of biological registries

Karel Pavelka
Institute of Rheumatology and Rheumatology Clinic of Charles University, Prague, Czech Republic

Registries of biological therapies are strongly recommended by EULAR, FDA and EMEA for all biologicals used in rheumatic diseases and were established in nearly western states and US. Data from registries bring additional data on safety/efficacy in real clinical practise. I safety area registries have brought extremely important data in follow up of frequency of serious infections/tuberculosis/opportunistic infections in different parts of the world and have stimulated prophylactic screening of latent tb and also demonstrated efficacy of such screening. In establishing the risc malignancy/lymphoma registries brought different figures than metaanalysis of RCT.
In efficacy area have registry generally confirmed efficacy from RCT in real clinical practise. Registries have added information on adherence to therapy and survival on individual treatment courses, efficacy of switching to other biological drug, prediction of response to therapy, evaluation of different sequences of therapy data from clinical subsets of RA, long-term efficacy and necessity to dose increase.
The registry ATTRA was founded 2001 and up to now data on 1200 patients with RA were included. It is nation-wide registry, when > 90% of patients are included. The registry of strongly oriented on efficacy and cooperate also with health-insurance in question on reimbursement. The patients are followed for radiographic progression, quality of life, ability to work.
Some main in ATTRA results: The means DAS28 drops from 6, 6 to 4, 2 and clinical response is achieved are 70-80% of patients. Survival on therapy after 1 year is 80% with gradual decrease. There may be differences in survival on individual anti TNF, when survival on ETN was significantly Langer than on other anti TNF. Radiographic progression have been delayed significantly after anti TNF (0,5-0,6 TSS/year) compared to estimated yearly progression before anti TNF therapy (7-8 TSS/year). The quality to life have been imported after anti TNF (Eurequol HAQ) and this altogether have been maintained in long-term.
7 cases of tb has been identified and based on this case and on study with quantiferone new guidelines for prevention of latent tb have been developed.

New approaches of glucocorticoid and NSAID therapy in inflammation

Pál Géher
St. John of God Hospital;
Semmelweis University, Budapest, Hungary

It is already 60 years ago when GCs were first used for the treatment of rheumatoid arthritis. Since that GCs are the most commonly used anti-inflammatory and immunosuppressive drugs in many disorders.
In 1985 the human glucocorticoid receptor (GR) cDNAs were first cloned, also the GR protein was analysed, in 1991 the receptor gene structure was elucidated.
The molecular basis of the mechanism of GCs:
– genomic action;
– non-genomic action;
– membrane-bound GR mediated non-genomic action;
– non-specific, non-genomic action.
There are several way to reduce the side-effects of GCs without loosing their therapeutic efficacy:
– selective glucocorticoid receptor agonists (SEGRA), by inducing transrepression, but lesser extent transactivation;
– antedrug or prodrug;
– nitrosteroids;
– liposomal GCs;
– combination of GC with drug whom intracellular actions amplify the effects of GCs.
There are an increasing number of studies which show that GCs alone or part of any DMARD combination therapy are effective in the short term for symptomatic control of RA and are probably effective in retarding radiographic progression.
Salicylate the first NSAID, was discovered in the 19th century. After the discovery of the cyclo-oxygenase enzime system new selective NSAIDs were developed with targeted effect. Unfortunately their use is hampered by gastrointestinal, cardiovascular and renal side effects.
Nitric oxide releasing NSAIDs, are a new class of anti-inflammatory drugs generated by adding a nitroxybutyl or a nitrosothiol moiety to the parent NSAID with less upper gastrointestinal toxicity, with acceptable anti-inflammatory and pain reducing capacities.

Faculty

The received CV-s of the faculty members are listed in alphabetical order

Prof. Dr. László Czirják

László Czirják is the head of the Department of Immunology and Rheumatology in the University of Pécs. He is involved in teaching of rheumatology and clinical immunology for medical students (in Hungarian and English), and also a regular speaker in postgraduate courses in clinical immunology, internal medicine, and rheumatology.
Three years ago, as a board member of the EUSTAR (EULAR Scleroderma Trials and Research Group), he organized the first EULAR/EUSTAR educational course on scleroderma in Budapest. Last year he was elected to the general secretary of the EULAR. He is a member of the Editorial Board of Annals of Rheumatic Diseases and Clinical Experimental Rheumatology.
He is the head of the Hungarian National Board of Clinical Immunology and Allergology.
He is predominantly interested is the investigation of the clinical and immunological aspects of connective tissue diseases. His research group performs studies on the survival, disease activity and other clinical-epidemiological aspects of systemic sclerosis. He is a participant and organizer of several international multicenter clinical studies.

Prof. Dr. András Falus

Ordinary member of Hungarian Academy of Sciences
Office address: Department of Genetics, Cell- and Immunobiology
Semmelweis University H-1089 Budapest, Nagyvarad ter 4, Hungary

Education and degrees:

1970 Faculty of Biology, Eötvös Loránd University, Budapest
1983 Candidate of Sciences (Ph.D).
1990 Doctor of Science (DSc) Hungarian Academy of Sciences
2001 Member of the Hungarian Academy of Sciences

Appointments:

1970-1975 Eötvös Loránd University, Budapest,
1975-1994 National Institute of Rheumatology and Physiotherapy, Budapest
1994- Semmelweis University, Budapest

Fellowships, study visits:

1980-1981 Odense, Denmark (supervised by Prof. Sven-Erik Svehag)
1984-1986 Boston, USA (Harvard fellow, supervised by Prof. Harvey R. Colten)
1989 Osaka, Japan (visiting professor, supervised by Prof. Tadamitsu Kishimoto)
1991 Bern, Switzerland (supervised by Prof. Alan de Weck)

Awards:
Szechenyi Award from President of Hungarian Republic, 2006
Geoffrey B. West Award (European Histamine Research Society, 2006
Neumann Award for Bioinformatics, 2006
Kesztyüs Lorand award and medal for Hungarian Immunology 2005
„Scientist of the Year" in Hungary 2001
Arany János Foundation Award, 1998
Széchenyi professorial fellowship, 1997
Markusovszky award: 1996
Award of Hungarian Academy of Sciences 1995.

Teaching activity:
Medical biology (cell biology, genetics), immunology, medical genomics, bioinformatics
Postgraduate Programme leader in immunology and genetics of Semmelweis University Postdoctoral School
Chairman of Genomics Network lecture series from 2001

Research interest: Oncogenomics, histamine biology and allergogenomics, immuno-informatics (immunomics).
Recipient of domestic (12) and international projects (5) in the last 10 years.

Involvement in international scientific community:
Member of Henry Kunkel Society (Rockefeller University, NY)
Member of the board of European Histamine Research Society
Founder member of International Immunoinformatical Society
Transmitting Editor of International Immunology
Associate editor of Inflammation Research
Member of the Editorial Board of Autoimmunity and Immunomics Research
Permanent referee for other Journals (Eur. J. Immunology, FEBS Letters, J. Clin Invest., Melanoma Research, J. Invest Dermatology, Cancer Research, many Hungarian Journals)
National delegate in European Strategy Forum on Research Infrasctructures (Brusselles)
Chairman of 1st Conference of Basic and Clinical Immunogenomics, 3-7 October, 2004, Budapest, Hungary
Co-chairman of International Congress of Immunogenomics and Immunomics**,** October 8-12, 2006, Budapest, Hungary

Involvement in Hungarian scientific community:
Former president of Hungarian Society for Immunology
Former head of Immunology Committee of Hungarian Academy of Sciences
Member of the Board of Medical Science Committee

Patents: One in U.S.A (1999), one in Hungary (2005)

Scientometry:
Peer reviewed journal articles: 267, books: 7, book chapters: 23
Cumulative impact factors: ~720 , total citations: ~ 3000, H-index: 28

Dr. Peter Gergely jr.

Dr. Peter Gergely Jr. earned his medical degree in 1995 and his Ph.D. in 2004 at the Semmelweis University, Budapest, Hungary. As a Rheumatology Research Fellow, he was conducting translational research at the State University of New York, Upstate Medical University, Syracuse, NY, US from 1998-2001. He has completed fellowship trainings both in rheumatology and clinical immunology and allergology and has been appointed Attending Rheumatologist and Head of Molecular Biology at the National Institute of Rheumatology and Physiotherapy, Budapest. He is also a Senior Lecturer at the Semmelweis University where he has been involved in teaching medical students and rheumatology residents as well as Ph.D. students. Dr. Gergely`s main interest includes the genetics and cellular abnormalities of a wide range of autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus. The research work by Dr. Gergely on the pathogenesis and clinical aspects of autoimmune and metabolic rheumatic diseases has produced more than 40 scientific papers and reviews in leading peer-reviewed journals and he has authored or co-authored several book chapters on rheumatic diseases. He has received numerous awards such as the Fogarty Fellowship Award from the National Institutes of Health, US or the Bolyai Janos Scholarship from the Hungarian Academy of Sciences. At present dr. Gergely is on sabbatical from the National Institute of Rheumatology and from the Semmelweis University and serves as a Translational Medicine Expert in Autoimmunity for Novartis. Top 5 first-authored papers by Dr. Gergely include J Immunol. 2002; 169:1092; Arthritis Rheum. 2002; 46:175; Clin Immunol 2005, 116:124; Rheumatology 2006, 45:1194 and Autoimmun Rev 2006, 6:5.

Prof. Dr. Pál Géher

Pál Géher was born in 1950, Budapest, Hungary. In 1975 he finished the Semmelweis Medical University, Faculty of Medicine, in 1979 he was specialized in rheumatology and physiotherapy. He spent a 1 year grant of rheumatology in France (1980-1981), and several months grant of health care administration in US (1994, 1996).
He worked as a rheumatologist in the National Institute of Rheumatology (1975-1993), Haynal Imre University of Medical Sciences, Chair of Rheumatology (1995-2001, assistant professor) and in the St. John of God Hospital in Budapest (2002-; head of department). He also worked in the Ministry of Health (1993-1995 and 2001-2002) as head of departement, vice secretary of state. He is also professor of rheumatology and physiotherapy since 2003 (Semmelweis University, Budapest).
He obtained the Ph.D. title in 1988 (Medical and social consequences of ankylosing spondylitis). He obtained two grants (Ministry of Health, Hungarian Scientific Research Fund) and leads a Ph.D. subcourse (Immune and genetic factors in rheumatic diseases) at the Semmelweis University.

His main scientific interests is the etiology and clinical aspects of spondylarthropathies. Number of publication (peer reviewed journals): 98 Impact factor: 49,27 (incl. abstracts), citation index: 128.
He is member of the Hungarian Board of Rheumatology, „Assessment of Ankylosing Spondylitis" (ASAS), president of the Hungarian Society of Spine, vice-president of the Hungarian Association of Rheumatologists and Hungarian Association of Balneologists and the Hungarian League of Rheumatic Patients, treasurer of the International Society of Medical Hydrology, Climatology. He also the president of the Medical Chamber-Budapest.
He was awarded by the Pro Sanitate Award (1995 — Ministry of Health) and Belák Sándor Award (2004 – Hungarian Association of Rheumatologists).

Prof. Dr. Tibor T. Glant

Foreign Member of the Hungarian Academy of Sciences.
J.O. Galante Professor of Orthopedic Surgery, Rush University Medical center, Chicago, USA

Education: Medical University of Debrecen, Hungary M.D. 1968 Medicine
Medical University of Debrecen, Hungary Ph.D. 1980 Immunology/Histology
Hungarian Academy of Sciences, Budapest (Hungary) DMSc. 1988 Medical Sciences

Teaching: Over 5,000 contact hours with medical and Ph.D. students (Anatomy, Histology, Embryology, Biochemistry, Molecular Biology, Genetics).

Honors, awards and fellowships (major): Carol-Nachman Prize for Rheumatology (International Prize) Wiesbaden, Germany (1995); Honorary Member of the Hungarian Orthopaedic Society (2001) and Hungarian Society of Rheumatology (2003); "Honoris Causa" University of Pecs, Hungary (2003), Officer's Cross: The Order of Merits of the Republic of Hungary (2004); Elected Member of the National Academy of Sciences (Hungary; 2007); Pfizer Visiting Professorship in Rheumatology (2008).

Advisory, Editorial and Review Boards: Regular member of the NIH study sections; VA Merit Review Board and 12 Foreign (non-USA) Research Foundations. Editorial Board Member (was or current) 8 journals, including J. Biol. Chemistry (1994-1999), Cartilage and Osteoarthritis (2000- present) J. Bone Joint. Surg., Am (2002- present), Arthritis Res. Ther (2004- present).

Society membership: American Association of Anatomists; American College of Rheumatology; American Society for Biochemistry and Molecular Biology; Society for Matrix Biology; Orthopedic Research Society (USA), Osteoarthritis Society, Society of Bone and Mineral Res.

Meeting Organizer: 4

Section chair of national/international meetings: 26

Advisor/mentor of research fellows, Graduate (Ph.D.) students: 68
(mentorship for 14 Ph.D. students)

Peer-reviewed publications: 171 (159 listed in PubMed)
Book chapters: 19
Peer-reviewed abstracts: >350 (>150 podium presentations)
Invited lectureship/speaker: 55
Research Interest: Experimental models of RA and AS; autoimmunity, T-/B-cell homeostasis, Genetics of autoimmune diseases

Dr. Gabor Illei

Dr. Illei graduated from the University Medical School of Pécs in 1985. He started his career at the National Institute of Hematology and Blood Transfusion in Budapest followed by three years as a Postdoctoral Research Fellow at the University of Oxford in England from 1990-1993. He moved to the United States in 1993, where he completed a residency in Internal Medicine at the University Hospital, State University of New York at Stony Brook and a Rheumatology fellowship at the National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda. He is Board Certified in Internal Medicine and Rheumatology. He received a Ph.D. from Semmelweis University in Budapest and a Master's degree in Health Sciences in Clinical Research from Duke University. After completing his fellowship he became a staff physician and clinical investigator at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. In 2004 he joined the National Institute of Dental and Craniofacial Research, as Head of the Sjögren's Syndrome Clinic. His research interest focuses on clinical studies of systemic lupus erythematosus and Sjögren's Syndrome. He has been principal investigator on several clinical protocols evaluating novel therapies or the long-term effects of immunosuppressive treatments in SLE and in Sjögren's Syndrome. He has published over fifty papers and several book chapters.

Dr. Emese Kiss

Professional title: M.D., Ph.D., associate professor
Affiliations and offices:

2007- National Institue of Rheumatology and Physiotherapy
Departement: Clinical Immunology and Rheumatology Department
affiliation: Head of department

1985-2007 Medical and Health Science Center, University of Debrecen
Third Dept. Of Internal Medicine, Clinical Immunology Division
affiliations: associate professor (2004) — senior lecturer (1998) – assistant professor (1990) – clinical physician (1985)

Academic qualifications/board certifications:

2005 Reumatology
2004 Habilitation exam for the associate professor position (thesis: Chronic complications in SLE)
2003 Senior for Ph.D.
1998 Defense of Ph.D. thesis (Experiences in lupus with special regards to complement receptor 1)
1997 Allergology and Clinical Immunology
1990 Internal Medicine
1985 Graduation with „summa cum laude degreee" as medical doctor from Medical School of University, Debrecen, Hungary

Scientific activity:

Original papers: 107 (Impact factor: 123.78, citation: 128)
Abstracts: 58
Book Chapters: 38

Grants:

1999-2000 ETT (National Scientific Committee)
1999-2001 Mecenatura (from University of Debrecen)
2001-2004 OTKA (National Scientific Research Found)
2006-2008 ETT (National Scientific Committee)

Foreign language knowledge:

1997 Basic Russian
1984 Upper intermediate English

Membership in scientific committees:

2005- Hungarian Osteology and Osteoporosis Society (MOOT)
2003- Hungarian Association of Rheumatologists (MRE)
2001-2002 Brit. National Osteoporosis Society (NOS)
2000- EULAR/ESCISIT Standing Committee (mailing)
1999- EURO-Phospholipid Project Study Group
1987- Hungarian Immunology Society (MIT)
1987- Hungarian Association of Clinical Immunologists and Allergologists (MAKIT)
1985- Hungarian Internist Society (MBT)

Prof. Dr. Tore K. Kvien

Tore K. Kvien is head of the Department of Rheumatology, Diakonhjemmet Hospital and professor at the University in Oslo.
His major research interest is clinical, epidemiological and therapeutic aspects of rheumatoid arthritis and related diseases.
He has contributed with more than 230 original scientific articles in peer reviewed journals. The majority of publications during the last years are based on longitudinal data from Norwegian disease and treatment registers, but his research interests also focus on secondary osteoporosis, imaging modalities and ankylosing spondylitis.
He is the current Editor of the Annals of Rheumatic Diseases and is the immediate past President of EULAR.

Prof. Dr. Peter Lakatos

After studies in biology and chemistry, Dr. Peter Lakatos finished medical school at the Semmelweis University, Budapest, in 1981. He started his medical career at 1st Department of Medicine, Semmelweis University. Between 1989 and 1992, he worked with Prof. Paula Stern at the Department of Pharmacology, Northwestern University, Chicago. After that, he returned to the Semmelweis University but remained a faculty member at the Northwestern University until 1998. Currently, he is a full professor of medicine and head of the Clinical Research Laboratory at the Semmelweis University. Dr. Lakatos and his research group have actively participated in the development and introduction of biochemical and densitometric methods in the management and research of osteoporosis. In the 80's, he developed an osteocalcin radioimmunoassay among the first. He directs basic and clinical research programs in the field of metabolic bone diseases with a special interest for osteoporosis and thyroid hormone-stimulated bone loss. During the last decade, his major interest lies in the genetic background of metabolic bone diseases. Dr. Lakatos also conducts drug development studies. He has authored more than 250 full length scientific articles and book chapters. Among others, Dr. Lakatos acted as the President of the Hungarian Society for Osteoporosis and Osteoarthrology (1999-2005) and board member of the European Society for Calcified Tissues (1997-2007).

Dr. Burkhard F. Leeb

Date of birth: August 23, 1956, Vienna
Current position:

2001- Head 2nd Department of Medicine, Lower Austrian Center for Rheumatology; Endocrinology, State Hospital Stockerau, Austria.
Head 1st Department of Medicine, State Hospital Stockerau, Austria
1984-1989 Training in Internal Medicine (2nd Dept. of Medicine, Lainz Hospital)
1989 Specialization in Internal Medicine
1990-1999 Consultant 2nd Dept. of Medicine, Center for Rheumatic Diseases, Lainz Hospital, Vienna, Austria
1994 Specialization in Rheumatology
1998- Boardmember of the Austrian Society for Rheumatology,
1999- Director, Lower Austrian Center for Rheumatology Stockerau Hospital, Stockerau, Austria
2001 Director 2nd Department of Medicine, State Hospital Stockerau, Austria
2003- Director 1st Department of Medicine and vice-director, State Hospital
15. 11. 2006 Director, Karl Landsteiner Institute for Clinical Rheumatology

Society memberships: Austrian Society for Rheumatology (president-elect); Austrian League against Rheumatism; Austrian Delegate to UEMS; Austrian Society for Bone and Mineral Research; Austrian Society for Geriatrics; Austrian Society for Ultrasound in Medicine; Austrian Society for Internal Medicine; Professional league of Austrian Specialists in Internal Medicine; Society of Viennese Physicians; Co-chairman of the EULAR-ESCISIT Polymyalgia rheumatica subcommittee; Co-convenot EULAR task force for recommendations for the managementof hand osteoarthritis; Co-convenot EULAR task force for recommendations for the diagnosis of hand osteoarthritis; EULAR task forces for recommendations for therapy of hip and knee osteoarthritis; EULAR task force for recommendations for the diagnosis and management of gout; EULAR task force for recommendations for the diagnosis of knee OA; Chairman of the Austrian delegation to the 3eInitiative 2007/2008; 2008/2009; Editorial Board Journal für Mineralstoffwechsel; Editorial board Journal of Medical Sciences Research; Editorial board Aktuelle Rheumatologie (invited).

Prof. Dr. Wlodzimierz Maslinski

Wlodzimierz Maslinski graduated from Warsaw University in 1982. He was trained in the Institute of Hematology, Institute of Biochemistry and Biophysics Polish Academy of Sciences, Institute of Rheumatology — Warsaw, Arrhenius Laboratory – Stockholm, University — Sweden, Harvard Medical School (Boston, USA). His main scientific interests are immunology and experimental rheumatology with special focus on the cytokine network, chronic inflammation and natural mechanisms regulating the immune response. Ongoing research carried out in the Institute of Rheumatology, Warsaw, Poland, highlights the role of bone marrow compartment in the pathogenesis of rheumatoid arthritis. The results of his research have been published in more than 120 publications. Present position: Chairmen of Department of Pathophysiology and Immunology and Scientific Director, Institute of Rheumatology, Warsaw.
Since 2004 he was elected as a President of the Polish Society of Rheumatology. He received Honorary Membership of Czech Society for Rheumatology. Editor of Central European Journal of Immunology (since 2000) and member of Editorial Board of several journals.

Prof. Dr. Karel Pavelka

Born: 1954 in Prague, Czech Republic

Present appointment and address:

Director of the Institute of Rheumatology in Prague (since 1991)
Head-chair of Rheumatology, Institute for postgraduate medical education in Prague
Head-chair, Clinic of Rheumatology, 1st Medical Faculty of the Charles University, Prague

Previous appointment and experience:

Research Institute of Rheumatology (from 1981)
Institute for postgraduate medical education in Prague (from 1986)
6 months at the rheumatological department of Prof. Müller in Basel (1988), Course for managements, USA; Short-term trainee on University in Miami, Malmö and Bristol

Publications, society membership:

Co-author of 10 monographers, 368 publications
Member of the editorial board of 10 rheumatological journals, deputy chief editor of Czech Rheumatology
President of Czech Rheumatological Society

Other activities:

Honorary membership New York Academy of Sciences; Honorary membership Czech Medical Society; Honorary membership Russian Society of Rheumatology; Honorary membership Slovak Society of Rheumatology; Honorary membership Czech Rheumatological Society; Honorary membership Polish Rheumatological Society; Honorary membership European League against Rheumatism; Head of Bone and Joint Decade program 2000-2010; Main organiser of 3rd Postgraduate Course of Rheumatology EULAR, Prague, 1997, 2004; Co-organiser of Conference of New York Academy of Sciences, B-cell and autoimmunity, Prague 1996; Co-organiser of Central European Congress in Rheumatology — Piešťany, Warsaw, Budapest; Main organiser – bilateral meetings Czech Rheumatological Society and Austria, Germany, Poland, Slovak; President of EULAR Annual Congress, Prague 2001; Organiser of Central European Congress in Rheumatology — Prague 2008

Prof. Dr. Andras Perl

Andras Perl received his M.D. and Ph.D. degrees from Semmelweis University in Budapest, Hungary. He was trained as a resident at the 2nd Department of Internal Medicine at Semmelweis and as a fellow at the University of Rochester. He held faculty positions at Semmelweis, the University of Rochester, and SUNY/Roswell Park Cancer Institute. He has been Professor of Medicine, Microbiology and Immunology since 1997, Chief of Rheumatology since 2001, and co-director of the MD/Ph.D. Program since 2003 at the SUNY College of Medicine In Syracuse, New York. His research has been focused on interactions of viruses and the host genome and signaling pathways that underlie T-cell dysfunction in lupus and models of autoimmunity. His laboratory cloned the HRES-1/Rab4 gene and mapped its lupus-linked genomic haplotypes at chromosome 1q42. He detected and cloned the human transaldolase (TAL) gene and identified it as a controller of the pentose phosphate pathway, glutathione metabolism, and mitochondrial hyperpolarization (MHP), a novel checkpoint of T-cell activation and apoptosis. Lupus T-cells exhibit MHP and ATP depletion which underlie in abnormal activation and death signaling. He developed knock-out mice which have cell type-specific mitochondrial dysfunction and model human TAL deficiency. His laboratory has published over 100 peer-reviewed papers, authored chapters in immunology and rheumatology textbooks, trained over 30 Ph.D. and postdoctoral students, and received funding from the National Institutes of Health, the National Multiple Sclerosis Society, the Arthritis Foundation, the American Lupus Society and the Alliance for Lupus Research. He was listed among the Best Doctors in Central New York and Best Doctors in America in 2007 and 2008.

Prof. Dr. Gyula Poór

Dr. Gyula Poór graduated from the Semmelweis University, Budapest in 1977. He started his medical career at the National Institute of Rheumatology and Physiotherapy, currently he works as the director general of the Institute.

He was conducting research on osteoporosis with L. Joseph Melton at the Mayo Clinic, Rochester, MN between 1992-1993. After returning home he launched the National Osteoporosis Programme in Hungary, along with others. Between 2001 and 2006 he was invited to join the World Osteoporosis Programme of the WHO, as rapparteur.

He is full professor of rheumatology at the Semmelweis University and the leader of the Postgraduate Rheumatology and Musculoskeletal Chair of the Medical University, Targu Mures, Romania, functioning in Budapest. He acted as the president of Hungarian Society for Osteoporosis and Osteoarthrology between 1993-1999, at present he works as the president of Hungarian Association of Rheumatologists

and as the editor-in-chief of the journal Hungarian Rheumatology. He serves in two boards for the Hungarian Academy of Sciences.
His major interest lies in the research of metabolic and inflammatory rheumatic disorders. His molecular research group published a lot of papers on the genetic background of these conditions and won several international and national grants. Dr. Poór authored more than 300 scientific articles, book chapters and books and was honoured with professional awards.

Prof. Dr. Yehuda Shoenfeld

Dr. Yehuda Shoenfeld is the head of the Department of Medicine since 1984, and he has founded and is heading the Center for Autoimmune Diseases since 1985 — at the largest hospital in Israel — the Sheba Medical Center, Tel Hashomer, which is affiliated to the Sackler Faculty of Medicine in Tel-Aviv University. Dr. Shoenfeld is the Incumbent of the Laura Schwarz-Kipp Chair for Research of Autoimmune Diseases in Tel-Aviv University.
His clinical and scientific works focus on autoimmune/rheumatic diseases, and he has published more than 1300 papers in journals such as New Eng J Med, Lancet, Proc Nat Acad Scie, J Clin Invest, J Immunol, Blood, J Exp Med, Circulation, Cancer and others. He has authored and edited 10 books, some of which became cornerstones in science and clinical practice, such as "The Mosaic of Autoimmunity", "Infections and Autoimmunity" and the textbook "Autoantibodies" all of which were published by Elsevier and sold by the thousands. He is on the editorial board of 25 journals in the field of rheumatology, and autoimmunity and is the founder and the editor of the IMAJ (Israel Medical Association Journal) the representative journal of science and medicine in the English language in Israel and also is the founder and Editor of the Autoimmunity Reviews (Elsevier). He has written more than one hundred chapters in books. Dr. Shoenfeld received in Vienna, Austria, the EULAR prize 2005: "The infectious etiology of anti-phospholipid syndrome". Dr. Shoenfeld has educated a long list of students being heads of departments and institutes.

Prof. Dr. José António Pereira da Silva

Date of birth: May 10th, 1957. Professor of Internal Medicine and Rheumatology at the University of Coimbra in Portugal. Ph.D. degree in the University of London in 1993. Higher Doctorate (Aggregation) at the University of Coimbra with a thesis entitled: "Teaching and learning Rheumatology: a cry for better tools".
Currently Member of the Editorial board of Acta Reumatológica Portuguesa, Annals of the Rheumatic Diseases, Clinical and Experimental Rheumatology, Clinical Rheumatology, Future Rheumatology and Best Evidence and Practice Clinical Rheumatology.

Chairman of the EULAR Standing Committee for Education and Training and member of EULAR Executive and Scientific Committees from 2001 to 2005. President of the European Board of Rheumatology (Section of the European Union of Specialist Physicians), as from December 2006.
Current research interests: Neuro-endocrine-immune interactions; osteoporosis; pain physiology and management.

Dr. Zoltán Szekanecz

Professional title: M.D., Ph.D., D.Sc.
Associate Professor of Medicine, Immunology and Rheumatology, Institute of Medicine, Head of Rheumatology Division, University Medical School of Debrecen
Highest education: University Medical School of Debrecen, Hungary (1982-1988); graduated as M.D.
Speciality: Internal Medicine (1994)
Immunology and Allergology (1998)
Rheumatology (2001)
Ph.D. thesis: "Cell adhesion molecules and cytokines in leukocyte-endothelial interactions" (1995)
D.Sc. thesis: "Recent data on the pathogenesis of rheumatoid arthritis: clinical Relevance" (2001)
Professional experience:
7/2001-present: Head of the Rheumatology Division, University of Debrecen Medical Center
9/1988-present: M.D., Ph.D., Associate Professor, Researcher, Institute of Medicine, University Medical School of Debrecen, Hungary
1/1993-12/1993: Research Associate, Department of Medicine, Arthritis Section, Northwestern University Medical School, Chicago, Illinois, USA
Editorial service:
Reviewer for Arthritis Rheum, J Bone Spine, Journal of Rheumatology, Rheumatology (Oxford),
Founder and editor-in-chief for Magyar Immunológia (Hungarian Immunology)
Publication activity:
Original papers: 159, total impact factor: 236, citation index: 1026, book chapters: 35

Prof. Dr. Anthony D. Woolf

Professor Anthony Woolf is professor of Rheumatology, Institute of Health Care Research, Peninsula College of Medicine and Dentistry, Universities of Exeter and Plymouth; Visiting Professor Faculty of Medicine, Lund University and Consultant Rheumatologist at the Royal Cornwall Hospital, Truro, UK. He is also Director of Research and Development for the Royal Cornwall Hospitals Trust and Clinical Director of the Peninsula Comprehensive Research Network.

He qualified from the London Hospital Medical College and trained in rheumatology at Hammersmith Hospital, Guy's Hospital, Royal National Hospital for Rheumatic Diseases and Bristol Royal Infirmary.

He is a clinical academic rheumatologist with special interests in the impact of musculoskeletal conditions, the management of musculoskeletal conditions, medical education and osteoporosis. He is involved in various initiatives to raise awareness of the burden of musculoskeletal conditions and raise priority for education, prevention, treatment and research nationally and internationally. He has written variously on burden of musculoskeletal conditions, medical education, viral arthritis and osteoporosis. He coordinated the European Bone and Joint Health Strategies project and edited WHO Report on the Burden of Musculoskeletal Conditions. He is Editor-in-Chief of Best Practice and Research Clinical Rheumatology; a founder member of the Bone and Joint Decade 2000-2010; was a longstanding member of the Exec Committee of the National Osteoporosis Society UK, including Chairman, and has been a longstanding member of the Exec Committee of EULAR, as Chair of the Education and Training Standing Committee and as International Liaison Officer.

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