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Competence Network Rheumatic Diseases

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1. Main aims of the network

Starting in 1999, the Competence Network has created a multidisciplinary national consortium devoted to excellence in basic, clinical and health care research in the field of rheumatology in Germany. One of the major aims has been to build up and further develop close and sustainable collaboration among and between researchers and clinicians. Today, the Competence Network Rheumatology is an internationally recognised research structure and has put Germany in a favourable position in the competition for European research grants. Crucial elements of this progress were the development of horizontal and vertical networking structures, a central network management, funding of individual research projects, research coordination, joint data bases and biobanking, a uniform communication platform and intensive PR work.

While in the 2nd funding period, from 2003 – 2004, individual projects were funded with results outlined in last years report, from 2005 federal funding was reduced to projects dealing with the completion and the maintenance of material banks, projects of the health services research section and the funding of the central structures. However, since the researchers participating in the Network were able to raise funds from other resources such as the German Research Foundation, the German Ministry for Education and Research or EU grants, the collaboration was maintained and extended aside the grants given by the Network. Based upon a decision in the coordination committee and the existence of externally reviewed and funded projects, new groups were also integrated. An important stimulus for research was set by the funding programme of the DGRh in 2005.

The specific **scientific aims** of the Network for the time period 2005 – 2007 have been

- ▶ to monitor the outcomes of current health care
- ▶ to develop evidence-based guidelines for diagnosis and therapy
- ▶ to identify markers allowing a prognostic classification of rheumatic diseases
- ▶ to identify markers predicting success of therapy
- ▶ to develop concepts for cell-based, curative therapies

Large patient databases were continued and further developed in order to monitor longitudinally disease

outcomes and health care provision. The German national databases for adults and children with inflammatory rheumatic diseases are internationally unique. They provide sound information on the processes and outcomes of rheumatologic health care in the era of new therapies and the ongoing changes in the health care system. The databases were transformed to IT data entry, and funds from other sources (industry, arthritis centres) were successfully acquired. The continuation in 2008 is secured. Cohorts built up in the second funding period were followed-up and completed. Sound methodology has been guaranteed by central biometrical advice.

The evidence based guideline on the management of early rheumatoid arthritis was updated and released in a second edition in 2007. Guideline development and integration of EBM into medical education and training will be continued in collaboration with the 'Rheuma Academy', an institute for continuing medical education set up by the German Society of Rheumatology (DGRh).

The investigation of cellular and molecular markers for the susceptibility to and severity of several inflammatory rheumatic diseases has been one focus of the basic and clinical research of the Network in the past. Impressive progress has been made, e.g. the discovery of HLA DPB1 and RXRB alleles predisposing for Wegener's granulomatosis, the identification of particular prognostic collagen-specific autoantibodies in RA, and of peripheral plasmablasts predicting SLE. New serological parameters in early RA were identified. The biomaterial banks established within the Network are critical prerequisites of this research. As new technologies become available to the Network, this work will continue to be a focus. By transcriptome analysis a global view on gene expression of cells involved in the disease process, under therapy or not, becomes available. Vice versa, a global view on autoantigens recognized in particular in rheumatic diseases by autoantibodies, does define an (auto)'immunome'. This entity appears to be a direct reflection of the patients etiopathogenesis and is probably of high prognostic value. Both approaches identify also genes of interest for predictive diagnosis and as therapeutic targets. The expression of these genes and proteins can also be monitored cytometrically on the single cell level. The exploration of preliminary data obtained so far in the various groups of the Network and the combination of postgenomic and

1. Main aims of the network

cytometric technologies will therefore be a prominent feature of our research in the forthcoming years.

Finally, the most ambitious aim of rheumatology research is the development of remission-inducing or even curative therapies. From the very beginning the Network has initiated the exploration of the ultima ratio therapy of complete immunoablation of rheumatic patients, followed by autologous stem cell transplantation. Although in a number of patients this therapy led to a complete remission of the rheumatic disease, which we consider an impressive proof-of-principle, the inherent risk of mortality, due to the long period of immunodeficiency, requires the development of much more advanced cell-based therapies. Such therapies will aim at the specific depletion of disease-controlling cells, while leaving the protective part of the immune system intact. As example, groups of the Network have identified CD20-negative, long lived, autoantibody-secreting plasma cells as a targets for cell-based therapies. Still other targets are T helper lymphocytes, probably controlling chronic immune reactions, a question analysed by groups in Erlangen, Leipzig and Berlin. Moreover, groups in Jena and Berlin have started to analyse the potential of using regulatory T helper lymphocytes (Tregs), with the potential to downregulate immune reactions, for the control of rheumatic inflammation.

Finally, recent advances have supported the development of research focusing on the different mesenchymal cells such as fibroblasts, osteoclasts and chondrocytes being additional key drivers in immunological processes in rheumatic diseases, studied by various groups in Münster, Giessen/ Bad Nauheim, Erlangen, Jena and Regensburg.

By virtue of the Network, the improved overall quality of research on rheumatic inflammation has qualified the Network scientists to compete successfully for and partner in national and international grant consortia.

Aims to sustain the Network

In 2004, the Network was formally integrated as a section ('Arbeitsgemeinschaft') into the DGRh. The federal funding of the central structures in the third funding period were crucial for the successful integration and the establishment of sustained structures. As an important signal for the full integration of the Network, the DGRh decided in 2005 to provide research grants (300.000 Euro in total) to researchers in the Network. After a competitive application procedure and external review five projects were funded.

From 2008 onwards, the coordinating structures created for the Network will be maintained within the central management office of the DGRh. An industrial forum of companies associated with the DGRh comprising so far 24 members has provided unconditional grants for the core structure of the central office via their membership fees. Additionally, they have supported the national database with annually 160.000 Euros in 2007 and 2008.

To further sustain the activities of the Network a research foundation ('Rheuma-Stiftung') is about to start its work. It will be run jointly by the DGRh and the patient organization Rheuma Liga. A concept for public fundraising has been developed in order to become independent of federal funding and industry support. This is seen as a long-term goal with expected revenues in 3–4 years. As soon as the foundation has raised a notable amount of money, research grants will be offered.

2. Horizontal networking

2.1 Scientific highlights of the research sections

2.1.1. Health services research section

Speakers: Dr. Jan Huelsemann
Prof. Dr. Matthias Schneider

The members of this research section have closely collaborated with a large number of clinicians within the Competence Network and the Collaborative Arthritis Centres. They have contributed to better knowledge of the current health care situation of patients with arthritis, on the costs of rheumatic diseases, and the adequacy of care on the population level. New funds for cross-sectional tasks such as the national databases were acquired. All publications from the projects described below are listed in Annex I.

National database of the German Arthritis Centers (project B2.1, Zink)

The national database has strengthened its role as the major resource of information on healthcare and burden of illness in the rheumatic diseases in German rheumatology. It has continuously been further developed and contains now all important disease-specific outcome measures. It has been used as a tool for quality assessment in the participating sites due to the provision of individual data analysis in contrast with the other participants.

Since 2005, data entry is performed decentralised and IT-based. Since 2007, additional funds could be acquired from a consortium of 12 pharmaceutical companies which are being used to pay for study nurses in the participating rheumatological practices and clinics.

DocuMed.rh, the modular medical documentation software designed for the German national database, is actually used by 20 private practices and 20 hospitals. It can be downloaded from the web (<http://www.rheumanet.org/DocumedSupport/>). The use is supported by comprehensive handbook and by hotline. To increase user value and acceptance modules for statistical evaluation were implemented, the interfaces to clinical information systems and medical practice management systems were extended in co-operation with software companies and agents and external data depositories (e.g. laboratory

information systems and picture archiving and communication systems) via web services were integrated. Client access via mobile devices for patients and medical staff in clinical routine patient care and for home office activities was developed.

Regularly, developments and trends in health care have been reported to the scientific community. Due to a large power-point collection of the results accessible for participants via the Networks' homepage usage of the data in education and scientific meetings is widespread. Industry can use the power point presentation as well as data from the reports. Each company receives individual data analyses on their own products.

Pediatric database (project B2.2, Minden)

The pediatric rheumatological database is the major joint project of the German pediatric rheumatologists. With 45 participating pediatric rheumatology units recording more than 6,000 children per year it gives a comprehensive view of the patient spectrum and the health care in pediatric rheumatology. The database has gained additional importance by offering disease-specific data-sheets for selected rheumatic diseases as well as tackling topical tasks through add-on modules or additional question batteries (e.g. costs, ocular involvement, vaccination coverage, complementary and alternative medicine use, etc.). Results were transferred back via individual data analyses and publications.

Biometrical support to cohorts and clinical trials (project B3.1, Listing)

The availability and involvement of an experienced biometrical group was critical for the proper conduct of the cohorts and a number of randomised clinical trials. The biometrician helped in the preparation of study protocols, ensured that data were collected in a uniform, high-quality manner and approaches were harmonized. Data analyses were supported. Various investigator-driven, independent randomized clinical trials were performed in close collaboration with Prof. Sieper, Dr. Rudwaleit, Prof. Braun, Dr. Baraliakos. The clinical studies investigated the efficacy of TNF-alpha inhibitors, glucocorticoids, and methothrexate in ankylosing spondylitis. By comparing

2. Horizontal networking

the GESPIC cohort with data from the infliximab trial, first results on the impact of therapy on radiographic progression were gained.

The group is also involved in a BMBF sponsored randomised clinical trial on early induction therapy (Hit HARD) which takes advantage of the network structures. They contributed to the KKS initiative on SAS macros for clinical trials. The group is also active in the international ASAS working group.

Early rheumatoid arthritis cohort

(project C5.2, Westhoff)

The 3-year observation of 1.061 early RA patients was successfully finished in January 2006. With 916 patients completing the last follow-up, drop-out rates were low. Several questions pertaining on the association between early disease parameters and outcome were investigated and published or they are in progress.

Osteoporosis in patients with rheumatoid arthritis (RA): Prevalence, risk factors, problems in health care

(project C5.3, Raspe)

This cross-sectional study in nine rheumatologic centres investigated the prevalence of osteoporosis among 434 female and 98 male patients with rheumatoid arthritis. All patients were examined via the DXA method. 49% turned out to be osteopenic and 22% had osteoporosis at the lumbar spine and/or the hip. Osteoporosis was as frequent in men (20%) as in women (22%). Risk factors for osteoporosis were higher age, low body mass index, and intake of glucocorticoids >7.5mg/d. Deficits in antiosteoporotic treatment compared to current guidelines were identified.

The German Rheumatoid Arthritis Population Survey

(GRAPS; Westhoff)

Under the auspices of the Competence Network, a population survey on rheumatoid arthritis was conducted. The last population survey stems from 1989 and had found that only every second RA patient had ever reached a rheumatologist. Since then new drugs and therapy guidelines have been introduced. To assess the quality of contemporary healthcare, a 3-stage population survey was conducted. The TNS Healthcare panel was used to access the gen-

eral population (n = 70,112). To identify the RA cases, a screening questionnaire of joint symptoms and respective diagnoses was followed by a detailed questionnaire. Positive responders were asked to participate in a clinical examination at one of 83 collaborating rheumatologists (Sept. 2006 – March 2007). Rheumatologists had to assess each RA patient if he was cared for adequately.

41 RA patients were found in 317 clinical examinations (17 seropositive, 24 seronegative). Almost all of them had visited a rheumatologist at least once and about two thirds were still in rheumatologic care. An unmet need for DMARDs was seen in 20% of the patients. This pertained almost exclusively to seronegative RA patients. Widespread unmet need was seen especially with regard to physical therapies (41%). In one third of the RA patients further diagnostic procedures were advised; this again pertained almost exclusively to the seronegative cases. Further investigations are needed to understand why especially the seronegative RA patients were at risk of undersupply with DMARDs.

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2.1.2. Immunevasculitides research section

Speaker: Dr. Torsten Witte

In the research section 'Immunevasculitides' two banks with biological material were established and several studies were performed which are summarized here.

Clinical studies:

- ▶ In the 'LUKON' study, 43 SLE patients from 11 centers were randomized to be treated with either azathioprine or methotrexate to sustain remission after therapy with cyclophosphamide. The final evaluation of the study is currently being performed.
- ▶ In a parallel study, predictors for infections were evaluated in patients treated with cyclophosphamide. As a result of this study, the Freiburg Infection Risk Score (IRS) was developed and is now available in the internet.

- ▶ In the PREGO study, the efficacy of GnRH analogues to sustain gonadal function in females treated with cyclophosphamide was evaluated. 32 patients were recruited into the prospective study. The final evaluation is going on now.
- ▶ In the 'LEM' study 54 patients with Wegener's granulomatosis were randomized after induction therapy with cyclophosphamide to be treated with either 30 mg of leflunomide/day or up to 20 mg of methotrexate/week. Leflunomide proved to be significantly better in sustaining remission, so that the study was discontinued earlier than initially planned.

None of the clinical studies would have been possible without the multicenter character of the Network. In exchange, all of the results have been presented to all the members of the network and will help to improve and standardize clinical procedures and therapeutic decisions.

Material banks:

Two DNA banks were established, one with material from patients with ANCA+ vasculitides and a second with material from patients with SLE.

- ▶ 20 patients with Wegener's granulomatosis were recruited for the vasculitis DNA bank. Extensive characterization of risk genes of vasculitides is going on. So far, after genomewide microsatellite analysis, associations of Wegener's granulomatosis with the PTPN22 620W allele as well as with a gene in the chromosomal region 6p21.3 have been characterized.
- ▶ In the SLE genetics project, 420 SLE patients and as controls 105 patients with scleroderma and 220 with primary Sjögren's syndrome were recruited in collaboration with 7 university centers and several patient support groups. The bank is now being used for characterization of SLE susceptibility genes by three international and two German groups. Several genes associated with autoimmune disorders (Trex-1, ILT6, NKG2D, IRF-5) have already been described. ILT6 has been patented for diagnostics and treatment of autoimmune disorders.

Both of the banks could not have been established without the support of the competence net and the help of colleagues from other centers and patient groups.

Clinical applications of antineutrophil cytoplasmic antibody (ANCA) testing:

Strategies for ANCA detection have been established; quality assessment programs (evaluation of the performance of commercial kits); organisation of educational workshops (for personal from clinical laboratories and physicians) have been performed. Furthermore, 10 sera were sent to all the members of the section immunevasculitides for evaluation of presence of ANCA twice a year to standardize and improve ANCA tests within the Competence Network.

In the future, the members of the section immunevasculitides want to continue the successful collaborations and have decided to further enlarge the material banks and establish registers of patients with rare disorders such as Churg-Strauss-Syndrome, Hyper-Eosinophilic-Syndrome and Ormond's disease. Furthermore, an inception cohort of SLE patients has been started and a study to compare biopsy with MR tomography in diagnostics of giant cell arteritis is being planned.

2.1.3. Spondyloarthritis research section

Speaker: PD Dr. Martin Rudwaleit

Experimental spondyloarthritis (SpA) projects investigated the detection and behaviour of Chlamydia trachomatis:

- ▶ Detection of Chlamydia trachomatis by PCR: PCR technology for detection of Chlamydia DNA was refined, standardised, and ready to become a diagnostic tool but unfortunately, industry did not further endorse this important development.
- ▶ Detection and behaviour of Chlamydia trachomatis in monocytes: the cytokine profile in serum and synovial fluid in reactive arthritis was studied as persistent infection of monocytes with Chlamydia. These findings contribute to a better understanding of the interaction between host and Chlamydia trachomatis.

2. Horizontal networking

The core element of the SpA network within the Competence Network Rheumatology was the establishment of the German Spondyloarthritis Inception Cohort (GESPIC) which was initiated in late 2000. GESPIC is a nation-wide, prospective observational cohort on SpA patients with early disease with focus on axial SpA. The aim of this cohort was to study the course of the disease, assess socioeconomic aspects and identify predictors of a poor outcome. Altogether 21 centres included 750 SpA patients (n=632 adult and n=118 juvenile SpA patients and) SpA patients in GESPIC. The key features of GESPIC are the following:

- ▶ SpA-subgroups: AS: n= 246; axial SpA: n=266; peripheral SpA: n=73; reactive arthritis: n=30.
- ▶ Early disease stage: patients with very early disease were included: the mean symptom duration in AS patients was 5.4 yrs with the mean duration since diagnosis of only 1.3 yrs. As many as 46 % having a symptom duration < 5 yrs (mean 3.1 years). Among axial uSpA patients, symptom duration was only 2.7 years (all had symptoms <5 yrs) and duration since diagnosis was 0.95 yrs. Such AS cohort with short disease duration is worldwide unique.
- ▶ High disease activity in early disease: both AS patients and axial uSpA patients had comparable disease activity (mean BASDAI 4.0 vs 4.1) while function (BASFI 2.4 vs 3.2) and spinal mobility (BASMI 1.1 vs. 2.0) was better in axial uSpA than in AS. Persistently high disease activity: Over a period of 1 year of follow-up as much as 31% of AS patients had a BASDAI \geq , and also 31% had an elevated CRP.
- ▶ Radiographic progression: in AS and axial uSpA patients, radiographic progression has been assessed after 2 and after 4 years. The two year datasets have currently been scored by two independent blinded readers according to the mSASSS and BASRI scoring systems. The rate of progression and predictors for poor outcome are currently being analysed.
- ▶ Cytokine and genetic studies: experimental projects associated with GESPIC related to cytokine and genetic studies. These studies confirmed the role of the TNF α -308 polymorphism. Yet, no other cytokine gene appeared to be relevant.
- ▶ Networking character of the cohort: The network of GESPIC centres served to conduct several clinical trials with anti-TNF agents and NSAIDs in AS. Further, diagnostic algorithms for early AS/axial SpA were developed based on GESPIC. This knowledge was transferred into daily clinical practice by numerous symposia, presentations at national and international meetings, and several publications in international but also national journals.
- ▶ Current status of GESPIC: the cohort is ongoing in 2007, pharmaceutical industry contributes 50% of the budget of the cohort after governmental funding was reduced by 50% in 2005. An official research application to the BMBF/DLR to continue and expand GESPIC has been formulated in July 2007 and is currently under review.

2.1.4. Rheumatoid arthritis research section

Speaker: Prof. Dr. Hendrik Schulze-Koops

Central to the research section is the establishment of a biomaterial bank from a multi-center nation-wide study on early rheumatoid arthritis (Harald Burkhardt, Frankfurt). Until now, three-year longitudinal observations on 354 patients with early RA (disease duration <1 year) are completed and DNA (~400) as well as serum samples (~1500) have been collected. The data and material bank serves as a platform for several projects in this research section. The samples have been recently relocated from Erlangen to Frankfurt as Harald Burkhardt, who is in charge of the bank, has moved to Frankfurt.

In collaboration with researchers in and outside the network sera, DNA-samples and clinical data were used to investigate new serological parameters of early RA, as well as genetic factors that are related to different aspects of the pathogenesis of RA.

- ▶ DNA-samples of the RA-inception cohort were made available to an external project (principal investigator: Prof. R. Straub, Regensburg) on genetic polymorphisms in the pathway of glucocorticoid metabolism after a respective application for the use of the material had been approved by the coordinating committee of the network. This study is still ongoing.

Other studies that were performed on the biomaterial of the RA inception cohort within the network resulted in the identification of

- ▶ RA-specific autoantibody responses to citrullinated collagen type II in > 40 % of patients with recent onset RA demonstrating the immunogenicity of posttranslationally modified cartilage constituents;
- ▶ an association of the SNP PTPN22*620W representing a functional mutation of a lymphocyte receptor associated phosphatase with the early humoral immune response to an arthritogenic B cell determinant in collagen type II. Moreover, a synergism of this predisposing genetic factor with the RA-associated HLA-DRB1 alleles ('shared epitope') on the early CII-autoantibody response could be demonstrated as well as its association with early joint erosions;
- ▶ the identification of a SNP on the IL-4 receptor that is highly predictive for erosive disease.

Current funding mainly permitted the maintenance of the biomaterial bank on early RA and the transfer of the bank from Erlangen to Frankfurt.

In order to increase the sample numbers in the bank, efforts have been undertaken to recruit samples from major private rheumatology offices throughout Germany. These efforts were successful in several places.

A major goal of ongoing research with the material from the bank is to identify prognostic markers for disease activity, the course of the disease (erosive vs. non-erosive) and the outcome of particular medical treatment. The material has contributed to several publications and patent applications. A second goal of the ongoing work is to link the database with a biomaterial bank of local joint pathology, that is currently developed by Thomas Pap, Münster.

Using the new biomaterial bank of local joint pathology, efforts are undertaken to standardize and certify local joint pathology at the level of EULAR standards.

The research section RA coordinates its efforts on the identification of biomarkers in RA with other federal funding programs, such as the national genome research network.

2.1.5. Experimental rheumatology research section

Speakers: Prof. Dr. Thomas Kamradt, Dr. Ulf Wagner

The projects in the research section Experimental Rheumatology have been focused on the pathogenesis of autoimmune diseases with a clear orientation on the physiology and pathology of the immune response.

Cellular therapy with regulatory T cells

(new project, Scheffold)

Progress has been made in the characterization and isolation of antigen specific regulatory T cells, which have been shown to profoundly suppress antigen-induced arthritis. The therapeutic potential of Tregs has been further enhanced by using defined subpopulations of Tregs with distinct functional characteristics, which suggests a highly attractive perspective to treat autoimmune diseases curatively.

Cytometric markers of thymic activity

(project C4.1, Radbruch)

The physiological mechanisms of immune reconstitution following complete immunoablation with autologous stem cell transplantation (ASCT) in severe treatment-refractory autoimmune diseases have been further investigated. Possible therapeutic modulation of the immune reconstitution following treatment could prevent recurrence of the disease.

2. Horizontal networking

CD27++ plasmablasts indicate recurrent SLE activity

(project C4.1, Radbruch)

The analysis of immune reconstitution of ASCT patients provided direct evidence that a drastic systemic activation of B and Th-cells, triggered by as yet unknown mechanisms, precedes clinical signs of SLE, including humoral autoimmunity. The role of different T and B cell populations has been analyzed with emphasis on the long-lived plasma cell pool of SLE patients.

Circulating CD27++ plasmablasts in rheumatoid arthritis patients

(project C2.2, Berek)

CD27++ CD19+ plasmablasts in the peripheral blood of RA patients have been shown to originate from germinal center reactions taking place most likely in the synovial membrane. The analysis of these cells allows investigation of antigen specificity despite the often limited availability of synovial biopsies.

Determination of genetic polymorphisms in RA-patients receiving biologicals

(new project, Kekow)

IL-10 promotor polymorphisms have been identified as genetic markers that determine the responsiveness to anti-TNF-alpha treatment in RA patients and are predictive for assessing the success rate of RA treatment with biologicals. The therapeutic responsiveness of patients to anti-TNF-alpha biologicals and the treatment continuation has been investigated in a large epidemiologic study.

2.1.6. Osteoarthritis research section

Speaker: Prof. Dr. Thomas Pap

The research section osteoarthritis was established in 2006, at the 34th annual meeting of the German Society of Rheumatology and initially involved experts (including rheumatologists, orthopaedic surgeons, pathologists and basic scientists) from 12 different academic centres, specialized hospitals and from ambulatory settings. The main agenda of this research section was defined as follows:

- ▶ establishing a multidisciplinary network of researchers interested in osteoarthritis
- ▶ improving the interaction of basic scientists and clinicians in studying the pathogenesis and new therapeutic approaches for the disease
- ▶ standardising the procedures of data and sample collection across the participating centres
- ▶ providing the basis for collaborative grant applications both at the national and international (EU) level for forthcoming osteoarthritis calls
- ▶ organizing common workshops as a platform of interaction between the different centres

Since the establishment of the research section, a database of interested centres and individuals has been compiled, and we have performed a survey among members of the German Society of Rheumatology as well as other interested individuals concerning their specific expectations. As a result of that survey, the group met at the 35th annual meeting of the German Society of Rheumatology and decided to initiate a research project that focuses on hand OA. A detailed plan of investigation, including a concept for potential funding, will be worked out and distributed for discussion and approval by the end of the year 2007.

2.2. Network publications

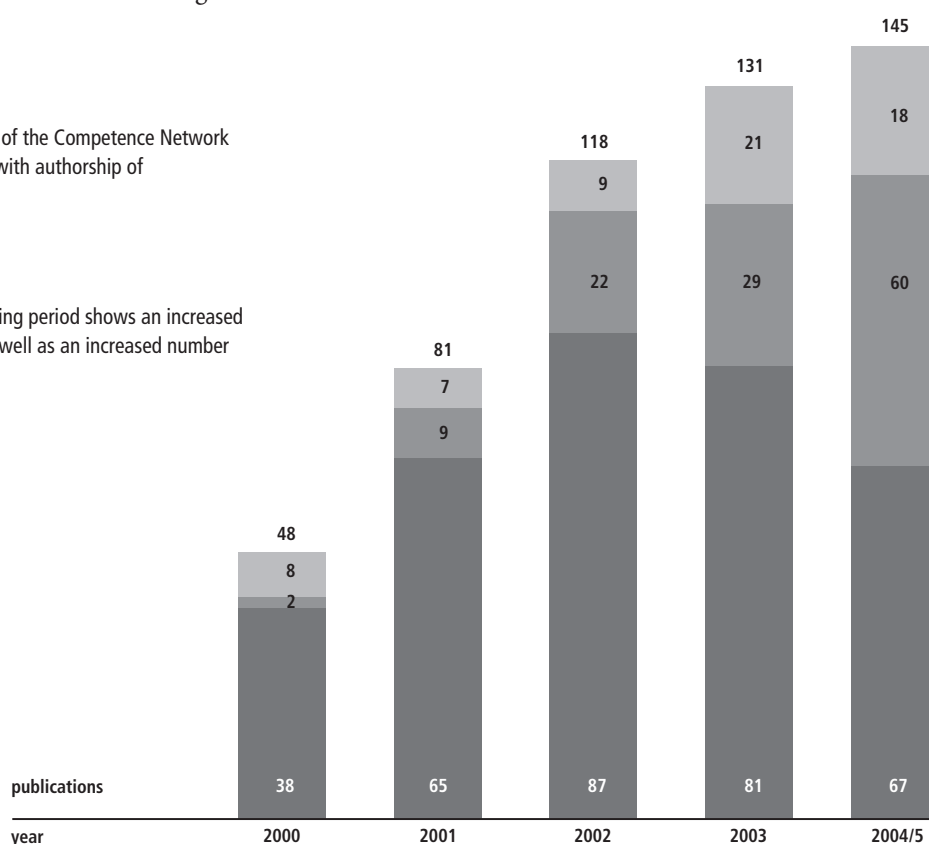
The number of publications of the Competence Network Rheumatology has increased continuously over the course of the funding periods as the figure shows the development from 2000 to 2004. Not only has the total number of publications risen but also the number of joint papers where 2, 3 or more members of the Network are involved. The vast majority of these publications have been published in international journals which demonstrates the excellence and quality of scientific results being achieved in the Network projects. Since the BMBF funding for most

of the research projects ended in 2005 the continuation of this figure is impossible. Accounting only the publications of funded projects results in a drop of the total number; accounting all publications of all Network members results in an huge increase – both methods do not represent the development. Therefore we made from 2004 onwards an analysis of all publications from BMBF-funded projects according to the ‘Science Citation Index’ (SCI) for the subject categories ‘rheumatology’ and ‘immunology’. The summary of the SCI analysis is shown in the table below; a complete list of all project-related publications is given in the Annex.

Output of publications from members of the Competence Network in 2000–2004, showing publications with authorship of

- one member or joint publications
- with 2 or 3
- and more members

Compared to 2000/2001, the 2nd funding period shows an increased output of cooperative publications as well as an increased number of total publications.



Year	SCI 15th percentile	SCI 25th percentile	other SCI publications	Total publications	Total Impact Factor
2004	14	22	18	63	161.057
2005	28	31	30	83	247.568
2006	31	32	26	67	247.404

Number of Network publications according to the ‘Science Citation Index’ for the subject categories ‘rheumatology’ and ‘immunology’ indicating the number of publications in the top ranked journals in the two left columns. Detailed information on Network publications is listed in the Annex.

2. Horizontal networking

2.3. Trial coordination

2.3.1 Overview of multi-center cohorts and clinical trials

Research Section Title of trial / project Principal Investigator, city	patients presently included	patients intended	network partners	recruiting university clinics	non-university clinics	recruiting private practices
Health Services Research						
C 5.1 Socioeconomic study: assessment of disease-related costs in RA. Ruof /Mittendorf, Hannover, completed	340	340	1	0	0	14
C 5.2 The influence of the intensity of rheumatologic care on the prognosis of early rheumatoid arthritis. Westhoff / Zink, Berlin	1061	1500	55	12	29	14
Immunevasculitides						
C 3.6 Validation of an INFECTION RISK SCORE (IRS) for SLE and Wegener's granulomatosis (WG). Peter / Miehle, Freiburg	40	ongoing	3	3		
C 4.2 LEM-Study: Leflunomide vs. Methotrexate (MTX) for remission in patients with WG, Project stopped. Voswinkel / Metzler, Lübeck	54	120	5	4	0	1
C 4.4 LUKON-Study (LUpus-KONSolidation therapies) Clinical Trial of efficacy and comparison of different consolidation therapies in SLE PREGO-Study. Manger / Manger, Wacker, Erlangen	43	100	11	6	2	0
PREGO-Study	32	24				
Rheumatoid Arthritis						
B 3.2 Prospective multi center study of early rheumatoid arthritis Burkhard / Kallert, Erlangen	369	400	15	5	6	4
Spondyloarthropathies						
B 3.3 Inception cohort on spondyloarthropathies Sieper/Rudwaleit, Berlin	750	open	11	3	4	4
Experimental Rheumatology						
C 4.1 Cellular Therapies for autoimmune diseases Radbruch / Kalden, Berlin / Erlangen	12		3	3		
Associated Studies initiated by the competence Network Rheumatology						
Long-term observation of treatment with TNF alpha inhibitors in RA Zink / Listing, Berlin	3154	4000	208	17	58	133
Multi-center study: Treatment of active ankylosing spondylitis with infliximab Sieper / Braun, Berlin / Herne	70	70	8	7	4	3
Placebo-controlled multi-center study: Treatment of spondyloarthropathies with sulfasalazine in Germany and Austria Sieper / Braun, Berlin / Herne	200	200	15	8	7	
Phase-III clinical trial of Etanercept in active ankylosing spondylitis Sieper / Braun, Berlin / Herne	30	30	2	1	1	
TNF-uSpA1: open pilot study: infliximab in active undifferentiated spondyloarthropathy Schnarr / Zeidler, Hannover	10	10	3	2	1	

2.4. Patient registers

Health Services Research Section Title of trial / project Principal Investigator, city	patients presently included	patients intended	network partners	recruiting university clinics	non- university clinics	recruiting private practices
B 2.1 National database of the German Collaborative Arthritis Centers (epidemiological study) Zink / Listing, Berlin	22.320 p.a.	open	62	20	29	20
B 2.2 National paediatric rheumatologic database (epidemiological study) Minden / Zink, Berlin	6.000 p.a.	open	45	21	17	6

For more details see report 2.1.1. Health Services Research Section.

2.5. Material and tissue banking

2.5.1. Overview of tissue and material banks

		patients actually included	patients intended status	recruiting university clinics	non- university clinics	recruiting private practices
Rheumatoid Arthritis						
B 3.2 Prospective multi-center study of early rheumatoid arthritis Burkhardt / Kallert, Erlangen	Blood (DNA, Serum), Synovial tissue	355	400	6	14	6
C 2.3 Novel markers for the diagnosis and stratification of RA* / ** Burmester / Feist, Berlin	Blood (DNA, Serum); synovial fluid and tissue	1600	2600	3	3	0
Spondyloarthropathies						
B 3.3 Inception cohort on spondyloarthropathies* / ** Sieper / Rudwaleit, Berlin	Blood (DNA, Serum, MNC), synovial fluid and tissue	750	ongoing	6	5	6
C 3.4 Development of highly-sensitive detection-methods for intraarticular bacteria in synovial fluid and tissue* Kuipers / Freise, Hannover	Synovia; further use: PCR optimization	842	ongoing	3	2	7
Immunevasculitides						
C 2.11 Genome-wide association study in ANCA associated systemic vasculitides: DNA- and EBV-lines bank Epplen / Jagiello, Bochum	Blood, EBV transformation of B cell lines; further use: genetic analyses	320	ongoing	2	0	0
C 2.12 Genetic risk factors of systemic lupus erythematosus* Witte / Schmidt, Hannover	DNA, Serum, EBV transformed B cell lines; further use: identification of SLE candidate genes	745	ongoing	7	0	50

* supra-regionally collection and central analysis

** The materials and material data are used as diagnostic reference samples. All material banks correlate their material data with medical patient records. The data processing is IT- based in all material banks

2. Horizontal networking

2.5.2 Collection structure

In the Network biobanking has developed at least partly in continuation of already existing banks that had been established in the collaborating competence centers based on their respective research traditions in different areas of scientific activities: rheumatoid arthritis, spondyloarthropathies, and immunevasculitides. Eight integrated material banks have been established. Due to the fact that already existing banks were continued, responsibilities are administered decentralized by the respective project leaders of the different banks. The central office of the Network receives updates of the inventory on a regular basis.

2.5.3 Material and data bases

The Network has several decentralized material banks which are handled according to local requirements. As examples, for two of the material banks specific details are listed here:

Rheumatoid Arthritis- Project C2.3

What material is collected?

PBMC preparation from patients with arthritis	n = 2600
Sera from patients with arthritis	n = 1000
Sera from patients with early arthritis	n = 230
Synovial fluid from patients with arthritis	n = 320
Synovial tissue from patients with early arthritis	n = 50

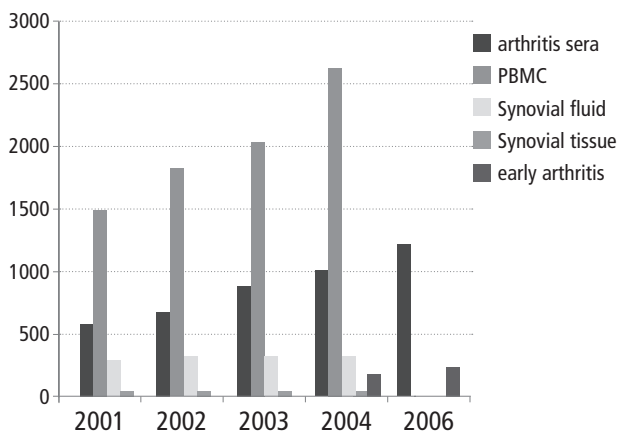


Illustration of the development over the last years in the RA biobank

Are controls included? Yes, from patients with other autoimmune diseases and arthritis.

How do you deal with biohazards? The samples are transported by messengers, no mail or official shipping.

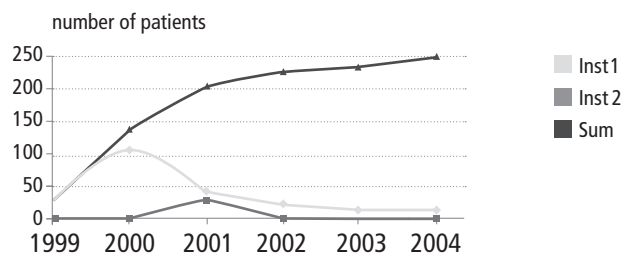
What is the database? The samples are encoded and stored separate and locked. The database is formatted in Microsoft Excel.

Does the database contain clinical, genetic or pathological Material banks correlate with clinical and pathological records? The database contains only clinical information.

Who does provide that input and where? Input is provided by clinicians and study nurses in the Charité hospital.

Immunevasculitides- Project C2.11

What data is collected? For the material database EDTA-anticoagulated blood has been collected by the respective cooperation partners. First, lymphocytes of blood of WG patients were separated by Ficoll gradient density centrifugation. In order to generate inexhaustible amounts of DNA (and RNA) B lymphocytes are subsequently EBV-transformed thus generating immortal cell lines. In addition to these tasks, the EBV-transformed B cells are cultivated for later use of DNA /RNA and other respective essays requiring living cells. So far, >320 patients with WG have been sampled.



Graphical illustration of the development of the number of WG patients during the funding periods from 1999–2004

Are controls included? Yes, the control subjects are summarised in an independent database.

How do you deal with biohazards? The bio-bank is stored in specially equipped labs (S2) with specific protection, e.g. for DNA preparation and immortalising of B-cells for cultivation.

What is the database? The data of our bio-bank are stored by two database computer-programs (Excel and File-maker) in anonymized manner in order to assure sufficient protection. In addition, these delicate data are saved in a specific 'file-server' which is secured maximally (firewall etc).

Content of the database? The clinical and genetic data are summarised in anonymous form in an excel- and file-maker-database. Thereby, it is possible to correlate our genetic analyses with the phenotypes represented by the clinical data of the cooperating institutes in a fast and efficient manner.

Does the database contain clinical, genetic or pathological information? The databases include both clinical and genetic data.

Who does provide that input and where? –The data are initially supplied by the respective clinical cooperation partners of the project. Clinical data are mainly collected at the vasculitis centre Bad Bramstedt and later on they are complemented with the genetic data at the department of Human Genetics (Ruhr-University Bochum).

Costs of the material bank and database in summary (2005–2006)? ~ 48,000 Euro.

2.5.4 Management of material banks

For a standardized handling of the data and material banks regulations have been developed. The formulation of these rules had to consider that quite a number of topics regarding biobanking including some ethical aspects, but especially legal questions concerning the proprietary and exploitation rights are rather complex. This complexity is illustrated by the fact that these legal aspects are still a matter of controversial discussions even in a special working group of the Telematics Platform of the BMBF despite professional advice by a specialized attorney. In conclusion, a pragmatic preliminary order for the use of biomaterial collected in the Network was enacted in autumn 2003 that will be replaced as soon as more generally binding legal conceptions are available. The preliminary order of biobanking is based on the following principles regulating responsibilities, rights and procedures:

1. Information of the scientific community

The Network publishes information on the existing biobanks including the names of responsible scientists and contact information for potential users on its homepage.

2. The responsibility of the administrator of the biobank

The scientist in charge is responsible for:

- ▶ Maintenance of its operativeness including proper handling of biomaterial (preparation, storage, shipment), appropriate documentation and data handling (electronic storage)
- ▶ Compliance with legal and ethical standards
- ▶ Reporting of the actual inventory to the central business office of the Network. An upgrade should regularly be given in 3 months intervals
- ▶ Timely processing of applications for use of biomaterial (compare item 4)

3. User rights

Who is allowed to use biomaterial?

- ▶ Internal use: for the approved Network projects, without any need for special application
- ▶ External use: academic institutions, companies, etc., a special application is required

4. Application procedure

The application has to be addressed to the scientist responsible for the respective biobank. The application should contain the following information:

- ▶ Quality and quantity of the requested biomaterial and eventually the accompanying pseudonomized data sets (clinical data, lab parameters, x-ray scores)
- ▶ Aims of the study. It should be possible to judge the application with respect to originality, feasibility, the intended use of the results (publication, patent, commercial use), and the chances for realization from the information given.
- ▶ A statement on data safety and ethical issues of the proposed project should be included.
- ▶ A statement concerning rewards (i.e. royalties in case of commercial use, or offers for co-authorship in case of intended publication) for the use of biomaterial should be included.
- ▶ Applications that do not contain information on all above mentioned items are regarded as incomplete and will not be processed until completion.

5. Decision procedure

- ▶ The scientist that is responsible for the biobank will have to formulate a judgment within 4 weeks after receiving a complete application (according to the specification in item 4) and to send this statement together with the application to the individual members of the coordination committee.
- ▶ The members of the coordination committee will decide immediately (without the necessity to meet each other) by simple majority of the votes. In case of equal votes the judgment of the scientist in charge of the biobank will decide.
- ▶ The coordination committee has the right to make the use of material dependent on additional requirements to be fixed in the material transfer agreements.

- ▶ The decisions of the coordination committee are binding on all parties. However, the scientist in charge of the biobank has the power of veto in few exceptional cases i.e. legal uncertainties in connection with the intended use of the biomaterial.
- ▶ All persons involved in the evaluation process have to deal with the information given in the application confidentially.

6. Material transfer agreement

The shipment of material is dependent on a prior signing of a material transfer agreement, that restricts the rights to use the material to well defined purposes, excluding any extension without separate application as well as the transfer to third parties. Depending on the respective project individual amendment statements will regulate the duties of the user with regard to exploitation rights.

7. Duration of validity

- ▶ In principle the regulations of biobanking will remain valid beyond the end of the BMBF-funding period since the Network will be integrated as a working committee into the DGRh. Thus the succession of the present coordination committee by an equivalent panel that will fulfill the task of supervision and decision making on the use of biomaterial collected in the Network is guaranteed. It will also remain the responsibility of the scientist in charge to guarantee the functionality of the respective biobank beyond the end of the BMBF-funding. In case that the administrator cannot comply with these requirements anymore it is his duty to actively contribute to a solution in collaboration with the supervising panel and to accept in this respect simple majority decisions. The panel has the right to withdraw the responsibility for the biobank from the administrator in the case that its continued existence is at risk.
- ▶ The enduring validity of the Network regulations will, however, allow for amendments to match standards that might be set in the future by consensus findings in working committees of the Telematics Platform, additional requirements by the BMBF or new interpretations of law concerning liability, proprietary and exploitation rights.

2.6. Cooperations with other research structures

The major activities of the research coordinator of the Competence Network are focussed on building European networks, acquisition of external European funding, and lobby work to increase the awareness and priority of rheumatic diseases within the EU. In the past years, intense communication and lobby work for topics in the Sixth and Seventh European Framework Programme (FP) was performed in collaboration with the National Contact Point for Life Sciences in Bonn. The CELLAID initiative (www.cellaid-eu.org) represents the successful integration of a specific topic and the corresponding grant application that was funded by the Sixth FP. Three symposia concerning 'Cell based therapies for autoimmune diseases' were held in Berlin, Brussels, and Florence, respectively. Scientific reports and summaries are published at the corresponding website. Specific topics like T-cell and B-cell targeted therapies, the role of cytokines and other cell types, and results from current innovative therapies with biologics were presented and discussed among European leading experts. Translational aspects, clinical status of ongoing trials, e.g. of stem cell transplantations, were discussed, leading to the necessary measures for pan European research projects and their clinical translation. At the second and third meeting, the participants also discussed the status of the Seventh European Framework Programme with officers from the European Commission. The CELLAID project is the platform for the preparation of specific topics to be called and applied for in the Seventh FP. A fourth Cellaid Symposium is planned to take place in November 2008.

For further lobby activities on the European level, the Competence Network cooperated with the European Science Foundation (ESF). Andreas Radbruch, Angela Zink, Cornelia Rufenach, and Jutta Steinkötter contributed to the coordination of a 'Science Policy Briefing Meeting' on rheumatic diseases, which was held 13–14 December 2005 in Brussels. An international expert panel, representing epidemiologic, basic, translational, and clinical research as well as the European League against Rheumatism (EULAR), European medicines agency (EMA), and patient representatives were invited. The result of this meeting, which was chaired by Andreas Radbruch and Maxime Dougados (Paris), is a statement on the potentials

and demands of research on all levels as well as networking on a European level. The statement will also present major recommendations for Science Policy and is directed to European as well as national funding institutions to support the progress in basic research and efficient translation into therapies. These tasks are of major importance to reduce the impairment of the patients' quality of life, to reduce the socioeconomic burden and to strengthen the European Research Area, support the development of innovative therapies and involved biotech and pharmaceutical companies. The final European Science Foundation Policy Briefing document 'Rheumatic Diseases – a Major Challenge for European Research and Health Care' (26 June 2006) stressed the importance of research in chronic inflammation, osteoarthritis, health care, and healthcare studies in the field of rheumatology as well as innovative therapies such as cell therapies aiming at long term remission and cure.

The Competence Network is further involved in the EU project AUTOCURE (www.autocure.org), which is an integrated project with high potential for success in the field of innovative therapies, validation, and clinical translation. Gerd Burmester, Andreas Radbruch, and Reinhold Schmidt are participating in the consortium. The German and European landscape of rheumatology research will benefit from the projects and results of the AUTOCURE project, which also includes training and demonstration events.

Starting in 2007, the coordinator supports proposals of specific topics according to the priorities of the Seventh FP.

Future activities on national and international level will include:

- ▶ Continuation of scientific workshops of the 'Forum Experimentelle Rheumatologie' and the Vision workshop as integrated elements of the annual congress of the DGRh
- ▶ Intensive lobby work towards specific calls and topics within the Seventh FP
- ▶ Ongoing cooperation with the ESF regarding European Science Policy and possible project funding through the ESF

2. Horizontal networking

- ▶ Grant application and support for applicants within the Seventh FP
- ▶ Continuation of the CELLAID initiative and series of symposia
- ▶ Continued coordinating activity for the AUTOCURE project
- ▶ Contact, communication, and integration with national and international networks in the field
- ▶ Continuous support for all members of the network and information service regarding external funding sources, national or European

Since activities have been increasing, e.g. in the course of the CELLAID project, in networking, and in preparation of new grant applications within the Seventh FP, the position of the research coordinator was extended to 40 hours per week. Especially with coordinating and writing grant proposals for the Seventh FP, the work load in 2007 made this extension necessary. Successful applications are of high importance for research in the area of rheumatology. Moreover, it is planned to finance the research coordinator after the third funding period by an EU grant.

3. Vertical networking

3.1 Main achievements

Cooperation with the regional collaborative arthritis centers:

By merging the central office of the Network with the central offices of the DGRh and the collaborative arthritis centers synergistic effects have arisen on all levels. Especially since the coordinator of the Competence Network is coordinator of the regional collaborative arthritis centers at the same time, the transfer of information onto the level of health care and into daily clinical practice has improved during the last three years steadily.

In 2007 the regional collaborative arthritis centers for the first time have announced an annual theme: 'Early diagnosis of rheumatoid diseases'. This topic is promoted throughout the year with main activities planned in October at the world arthritis day with actions in 25 arthritis centers all over Germany. The topic was chosen with the purpose to bring new results from the Network's research into the periphery. The information material was prepared on the basis of knowledge gained from the evidence-based guideline of early RA and the GESPIC cohort - both described in the next paragraph 3.2 on reviews and guidelines. For the campaign two flyers have been produced - one for general practitioners and one for patients with a wide distribution in pharmacies. The 'rheuma-check', an interactive test on the homepage was extended for questions regarding spondyloarthritis. The PR is supported by the Network with corresponding articles in the Newsletter, in the internet with chats and an interactive map. Numerous press articles accompany the campaign. In 2008 the annual theme 'patient education' will be promoted over the course of the year.

Public relations:

One of the central goals of the Network was to develop an information network extending from the research laboratory to the patient. This goal has been achieved with the employment of a medical journalist. Continuous press releases and regularly held press conferences have raised enormous attention for the Network in the press that is reflected in a great number of press reports about our work. The activities to maintain the information network covering interests from the research laboratory to the patient has been extended on different levels.

- ▶ Since the beginning of 2005 a newsletter of the Competence Network is produced on a quarterly basis which reports about activities in the Network, new diagnostic tools, and ongoing studies on innovative therapeutic procedures. This newsletter is widely distributed not only to members of the Network but also to patient organizations, rheumatologists and general practitioners, clinics, press offices, health insurances, governmental institutions etc. 'Guest' authors from other groups can place related topics and the feedback confirms that this as a successful concept for an interactive exchange.
- ▶ The major tool in PR work continues to be the internet as described in chapter 6 on visibility.

Cooperation with patient organizations:

Our Network is cooperating with self-help groups and other lay groups on different levels. The joint organization of local patient information events (symposia, workshops) as well as cooperation in studies is coordinated by the following two groups:

- ▶ Regional Collaborative Arthritis Centers
- ▶ 6 Competence Centers

Further cooperations on a supra-regional level:

- ▶ Integration of a section for collaborative projects into the internet platform with links and technical support.
- ▶ Regular exchange of information about activities for publication of new results from the Network in the patients magazine 'Mobil' and vice versa publications from the 'Rheuma-Liga' in the newsletter of the Network.
- ▶ Joint public relation activities such as information leaflets ('Why go to the rheumatologist') or common press conferences (e.g. European Alliance against arthritis and World Arthritis Day).
- ▶ Since 2003 a representative of the self-help group 'Rheuma-Liga' is member of the coordinating committee of the Network. The participation of a representative of the 'Rheuma-Liga' in meetings of the coordinating committee has already yielded valuable input for the 3rd funding period.
- ▶ A more intense cooperation with the German patient organization 'Rheuma-Liga' has started in 2004 with

3. Vertical networking

founding consumer advisory board with two meetings per year. To support this board the Competence Network covers the costs for these meetings. And the coordinator of the Network is a permanent member. In addition, members of the Network are invited to speak on special topics and discuss with the advisory board new developments and strategies for future research directions. The Rheuma-Liga has therefore started the process of getting involved also in basic research.

- ▶ Since the beginning of 2006 a peer group of 6 members both of the boards of the DGRh and the Rheuma-Liga has developed a concept for a research foundation to raise funds independent of governmental funding to support research projects in the future. This planned foundation is described in more detail in chapter 7 on sustainability.

Medical information for external groups:

The Network offers information for patients, family members, doctors and other professionals. A lot of these activities are organized by the regional centers which inform on their local homepages as well as leaflets about the offerings. The activities of Network members include:

- ▶ Participation in meetings of the Regional Collaborative Arthritis Centers to inform about the activities in the Network, new diagnostic tools, and ongoing studies on innovative therapeutic procedures. These meetings are usually open to doctors from all different specialties in hospital and private praxis as well as to general practitioners.
- ▶ For rheumatologists and interested internists or general practitioners a variety of medical education programs is available like special training courses with selected topics, quality circles, interdisciplinary seminars, and case report conferences.
- ▶ Special day or weekend seminars for patient information are organized most often in collaboration with lay groups.

Especially the internet with a variety of features helping patients and doctors to find specific information will be used extensively to transport medical information to external groups. Regularly updated medical information

for patients, relatives and doctors is provided by the Network on its homepage. Since 2006 all internet activities are joined with the DGRh.

More details are described in section 6 on visibility.

3.2 Reviews and guidelines

Development of an evidence-based guideline:

Management of early rheumatoid arthritis

The network developed the first S3 guideline in German rheumatology. According to the major deficits in patient care recognized by analyses of the national database of the Network this guideline addresses the 'Management of Early Rheumatoid Arthritis'. Our aim was to develop the guideline according to international and national standards, as they are recommended by the European Council, the German Agency for Quality in Medicine, the Association of the Scientific Medical Societies in Germany and the Scottish Intercollegiate Guidelines Network. Recent international efforts have been started to share resources and work. Founding and setting up the Guideline International Network (GIN) is a major step towards an international collaboration on this topic. In accordance with these international attempts we adopted a guideline from the Scottish Intercollegiate Guidelines Network (SIGN) and tailored it to the needs of the German health care system. The original SIGN guideline 'Management of early Rheumatoid Arthritis' was published in 2001. The guideline is targeted at the interface general practitioner-rheumatologist to support early treatment with Disease Modifying Antirheumatic Drugs (DMARDs). All relevant professional and scientific bodies involved in a multidisciplinary team care were invited to contribute and to nominate representatives for participation in the development group. This included also representatives from the patient organization 'Deutsche Rheuma-Liga'.

After a first review process the members of the guideline group decided to take the Scottish guideline as a master copy. The following rules for the revision process were set up by the group. Modification of the original recommendations if

- ▶ peculiarities of the German healthcare system make the original recommendation inapplicable,
- ▶ there is new evidence which makes an update of the literature search and the recommendations mandatory, e.g. new drug developments,
- ▶ the group had the impression that recommendations were insufficiently based, a link between evidence and recommendation was missing or the preliminary work was not done thoroughly enough.

In addition, all given recommendations were checked concerning their link with the supporting evidence. All publications cited as evidence base of the recommendations were critically appraised and classified according to their hierarchy of evidence and the resulting strength of recommendation. Additional literature search on specific German topics such as 'bath therapy' and 'in patient rehabilitative medicine' were performed.

As a result the outline of the original guideline was adopted. Within the chapter on medical therapies the order was changed to put more emphasis on the early start of DMARD therapy, the main message of our guideline. One major change as regards content is the different definition of "early rheumatoid arthritis", which included the first five years in the Scottish guideline and includes only the first two years in our version. Because of the different selection criteria this results in differences in the considered literature. 27 recommendations were formulated in our guideline, 10 of which were taken from the original. Five recommendations have the same content but different grades of recommendation, caused by recruitment of different studies or differences in the results of the critical appraisal process. Another 12 recommendations were newly formulated.

The German guideline has 178 citations of which 96 are included in the Scottish guideline also; the other 82 literature citations are different. The difference is mainly due to newly published studies and due to the fact that we included, whenever possible systematic reviews preferentially.

For the adaptation process we had expected that the major workload and needs for modification would be caused by the different situations in the two health care systems. In contrast to this we found that the major work was caused by reassessment of recommendations which was necessary because the link between the recommendation and the evidence was not explicit enough. Especially in cases where underlying evidence tables were missing this led to uncertainty and the demand to redo the literature search and the critical appraisal.

Collaboration in the field of guideline development will be strongly facilitated when the presentation of the recommendations and their underlying studies are as comprehensive as possible. Ideal tools are evidence tables, giving an ideal summary about the existing studies and their methodological quality. That enables an independent formulating of the recommendations. Without evidence tables adaptation of existing guidelines results in reproducing nearly the complete development process.

The guideline is available in the internet platform since fall 2004. The printed version booklet is available in the central office on demand. Furthermore, the index of practicing rheumatologists in the 'Praxis- und Klinikwegweiser' was used for the distribution of the guideline: all rheumatologists received an e-mail including the information that the final version of the guideline is online available. At several workshops and meetings the guideline was presented to the public and special audiences. The first update of the guideline was published in 2006.

German Spondyloarthritis Inception Cohort (GESPIC)

The core element of the SpA network within the Competence Network Rheumatology was the establishment of the German Spondyloarthritis Inception Cohort (GESPIC) as described in 2.1.2. With an international group of scientists (ASAS) under the guidance of J. Sieper and J. Braun diagnostic algorithms for early AS/axial SpA were developed based on GESPIC. This knowledge was transferred into daily clinical practice by numerous symposia, presentations at national and international meetings, and several publications in international but also national journals.

4. Network management

4.1 Achievements regarding infrastructure, quality assurance, organizational support and communication

Infrastructure

To secure sustained function of the Network during the 3rd funding period and afterwards, a major organizational measure has been installed recently: the integration into the German Society of Rheumatology (DGRh). The Competence Network Rheumatology is now integrated as a self-contained section ('Arbeitsgemeinschaft'; AG) into the German Society of Rheumatology (DGRh) since January 2005. As an AG of the DGRh, the Network will aim at coordinating and fostering excellent research in the field and at communicating this to the other organs of the society, in particular the Collaborative Arthritis Centers, which will form a parallel AG of the DGRh, and which will also provide the avenue to translate research into diagnosis and therapy. The statutes provide the frame to keep the Network dynamic and excellent, by inclusion of new groups upon external review and internal approval, and by exclusion of old groups, when they loose externally reviewed grants. The elected speaker of the Network is a member of the board of the society and represents the interests of the Network.

A joint Central Business Office has been set up to work for the Competence Network Rheumatology, the German Society of Rheumatology and the 'Association of Collaborative Arthritis Centers'. The central facility allows efficient coordination of activities by taking advantage of synergistic effects and overlapping tasks such as research coordination, workshop organisation, and acquisition of joint grants, which will ensure sustainability in the long run. Each of the partners financed 0.5 positions for coordination in the central office since 2005. After the BMBF funding the position of the coordinator will be financed in total by the DGRh as well as half of the position of the research coordinator. For internet and communication a part time coordinator will continue the the activities.

Quality assurance

Instruments implemented to assure the quality and efficiency of the collaboration within the Network include:

- ▶ Annual assessment of single projects by interim progress reports.
- ▶ Project controlling: All projects have defined milestones for the third funding period which are called to account in the progress reports and delays or divergences have to be explained. Milestones are controlled internally by the speakers of the Network and the speakers of the research sections.
- ▶ Regular meetings of the coordinating committee and the speakers committee provide control of the projects progress.
- ▶ Joint measures for scientific/methodological quality assurance: On the horizontal level six research sections have been implemented for scientific exchange and quality assurance. Each of them meets on an annual basis and submits a success report about its scientific progress, the cooperative results and any hindrances it has encountered in its attempts to enhance cooperation. Vertical cooperative results (common publications of experimental researchers, clinicians, epidemiologists or publications making direct use of resources on the patient-care level) are separately documented by the central office. Depending on the particular research section contributions of the individual Network partners to the central tasks of the Network are documented, including preparation of information for the internet platform, answering of questions from patients and family doctors, contributions to the central sample banks, participation in the national database and in multi-center studies, contributions to scientific conferences, organisation of advanced training for doctors and patients. Project B3.1 provides biometrical support for clinical cohort studies and secures methodological quality assurance.
- ▶ Joint measures for quality assurance of medical care: The Competence Network is cooperating closely with the German Society of Rheumatology (DGRh) for the development and adaptation of guidelines for medical care. Furthermore, project B2.1 evaluates rheuma-

tologic health care in Germany by running a national database in close cooperation with the German Regional Collaborative Arthritis Centers. The centers are distributed all over Germany and are responsible for provision of rheumatologic health care on the regional level.

- ▶ Mechanisms for the management of conflicts between Network members: Severe conflicts did not occur so far. If they may occur in future, conflicts should be managed by the coordinating committee or by the executive board of the DGRh.
- ▶ Mechanisms for the controlling of finances: Finances are controlled by the six competence centers themselves. The central and overall budget is determined in the coordinating committee. Central funds are administered by the central office.

Mechanisms for the acceptance of projects/dismissal of unsuccessful projects within the Network:

- ▶ Announcements about new objects of funding are being launched among rheumatologists in the German rheumatology journal 'Zeitschrift für Rheumatologie', in the quarterly newsletter, by mailings, in the internet and at the annual DGRh meeting as well as other workshops.
- ▶ For granting funding – e.g. the Start-up initiative of the DGRh in 2006 – an external board of international reviewers has evaluated the project proposals with respect to the scientific quality of the applications, relevance to the health services, networking and excellence of previous results.

Services, expert advice and support

- ▶ Biometry: The methodological approaches in all clinical cohort studies were harmonized. Biometric support in all research stages (writing of the study protocol, development of case report forms, organization of monitoring, data checking, quality control, statistical analyses) was given by the project B3.1.
- ▶ Clinical pharmacology: The Network is cooperating closely with the German Society of Rheumatology

(DGRh). Prof. B. Manger is spokesman of the commission pharmacotherapy in the DGRh that deals with therapy recommendations concerning e.g. the Cox2-inhibitors or TNF-alpha blockers.

- ▶ Coordination of clinical studies: Advice is provided by project B3.1 (Biometrical and organisational support for clinical cohort studies). In terms of organisation the central office supports the identification and acquisition of hospitals and rheumatologists for patient recruitment.
- ▶ Ethics: All studies have received ethical approval by the respective ethics committees. As far as ethical questions in collaboration with industry are concerned the Network relies on recommendations provided by the DGRh which launched the draft version in fall 2007.
- ▶ Human genome and gene technology: The rheumatology Network is associated to the German National Genome Research Network (NGFN 2) also funded by the BMBF. Partners from the competence center Berlin initiated a regional network for the functional gene expression analysis in systemic inflammatory rheumatic diseases in order to identify novel genes for diagnosis and therapy (BerlInflame). Additionally, the Network is associated to an initiative of the EULAR for functional genomics in rheumatic diseases, and several partners within the Network are associated to German and international research networks in this research area.
- ▶ Information and knowledge services: An IT platform for knowledge transfer, dynamic communication and online documentation with and within the Competence Network has been established with rheumanet.org. This platform serves as a structural and organisational instrument to facilitate vertical (between different layers of care and research) and horizontal (co-working of peers in different layers) networking in German rheumatology. Among the processing of a dynamic medical website and its maintenance, all basic functionalities have been prepared to promote the development of the so-called global net wide data dictionary (GNW-DD called Documed), to make it a sustainable instrument for web-based documentation. For more details see chapter 5 on IT-techniques.

4. Network management

- ▶ Media presentation: The central office and the journalist of the Network have developed several presentations of the Network that are available in the central office.
- ▶ Patents, funding and legal requirements: The central office provides advice in questions of patents and use of commercially interesting research results.
- ▶ Brokerage of general information: This is provided by the central office, the coordinators of the six competence centers and the Network's journalist in close cooperation with the internet platform and the newsletter as described elsewhere.

Communication procedures

All projects within the Network with 'cross sectional tasks' support the Network partners and offer services at different levels. These projects include the central business office (A5.4), public relations (A5.10), EDP-platform (B1), the biometry unit (B3.1) and the peripheral coordinators of the six competence centers (A5.1). Communication procedures implemented are:

- ▶ Organization of scientific and Network meetings: Most of the scientific meetings are now integrated into the annual conference of the DGRh. The 'Forum Experimental Rheumatology' takes place for the 9. time in 2007 and is a platform for Network members and international guests. The company Roche is sponsoring poster prizes in the Forum for young scientists. Established in 2005 the so-called 'VISION'-workshop is dedicated to a specific new technology, e.g. in 2007 RNAi technologies, where international guests are invited. All research sections meet the day before the annual meeting and additional scientific meetings are organized by the speakers of the research sections on demand.
- ▶ Provision of Network information: Since most of the Network members do not receive funding via BMBF for their research projects any more and therefore the annual reports of single projects are no longer available, the central office initiated a research data base in the internet in 2006. All members can sign up here with a profile of their research, describe the projects, list publications, funding, biomaterial, trials etc. A search function enables to screen for any wanted area. Due to technical problems in the development of the data base, we started in spring 2007 to enter the members information and are still in the process of building up. The database can be entered under <http://www.dgrh.de/forschungsdatenbank.html>. An annual update is planned among the members.
- ▶ This long-term financial support by the universities will be crucial to maintain the high standard of clinical research reached at the competence centers today. The major tasks of the six local coordinators at the universities of Berlin, Duesseldorf, Erlangen, Freiburg, Hannover and Luebeck in the future will be:
 - ▶ to participate actively in the research sections of the Competence Network
 - ▶ to coordinate research in the respective departments like randomised clinical trials as well as observational studies
 - ▶ to coordinate research applications for the participation in new research programs arising for example from the Road Map process of the BMBF, from the clinical research programme of DFG & BMBF or from the EU both on the local level and with other centers within the Network
 - ▶ to maintain the biobanks
 - ▶ to implement guidelines into daily patient care

4.2 Local clinical coordinators

One important structural element of the network is the coordinated interplay between the six competence centers. Local coordinators are mandatory to connect these centers among each other and to the central office as well as the local activities. From the beginning of the network til today the peripheral coordination offices have proven to be of immense value to realize the concepts. For the 3rd funding period requested funding has been reduced to 50% because all competence centers succeeded in acquiring the missing 50% from the respective university. From 2008 onwards it is planned that the local coordinators will be financed in whole by the universities.

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- ▶ to maintain the biobanks
- ▶ to implement guidelines into daily patient care

- ▶ to organise educational activities between rheumatology specialists and general practitioners
- ▶ to bring the results of clinical research back to patient health care as well as student education
- ▶ to support the Network activities by contributing to the Vision workshops, the internet activities ('topic of the month', chats, patient information etc.), and public relations.

The tasks of the research coordinator are described in more detail in chapter 2.6. on cooperations. The coordination of the well established 'Forum Experimentelle Rheumatologie' as well as the newly established VISION workshop are the national communication platforms of the network. In addition, a series of EU-funded workshops – CELLAID – have established an international network among high ranking international rheumatologists. Other activities in the 6th FP and lobby work for the 7th FP as well as co-organisation of an ESF workshop extended the tasks of the research coordinator immensely. Starting in 2007, the coordinator supports proposals of specific topics according to the priorities of the Seventh FP. With an interim financial support of the DGRh for the research coordinator the hope is to get at least one EU grant which will finance this position from 2009 onwards.

4.3 Promotion of young scientists

The Network has granted 15 fellowships in total (11 sabbatical and 4 rotation fellowships) in order to support scientific exchange among the competence centers (rotation) and to enable clinicians to work experimentally without clinical obligations (sabbatical). Results evolving from this work have been presented at conferences and some papers have been published. Due to financial restrictions we could not prolong the fellowship program in 2004.

Taking into account the importance of the support of young scientists we have now found alternative ways to prolong this activity. Funds of 300.000 Euro of the DGRh have been used for start-up research projects for young scientists in 2006. The aim of these fellowships is to support young scientists with new projects and research concepts in the beginning to enable them to publish and thereafter successfully apply for funds at other sources such as DFG or BMBF. An evaluation of this start-up initiative will take place in fall 2007 and we are hoping to readopt these successful activities in the future. In order to do so, the DGRh will set up a research foundation aiming to support research projects, development of clinical guidelines and concepts for medical education in rheumatology as described below.

In addition, we have granted travel fellowships to 12 young scientists in 2007 to present their data at international meetings. This activity will be continued with funds of the Arthur-Vick foundation.

Aollicant Holder	University / Clinic	Time Period / Exchange	Grant
Prof. Dr. Thomas Kamradt	University of Jena	Generation of B Cell retrogenic mice for experimental arthritis research	50,000 EUR
Dr. Elena Neumann	Kerckhoff-Klinik GmbH Bad Nauheim	Migration potential of synovial fibroblasts in patients with Rheumatoid arthritis	50,000 EUR
Dr. Marvin Peters	University of Münster	The role of SENP7 in the activation of rheumatoid arthritis synovial fibroblasts	50,000 EUR
Dr. Chiara Romagnani	Deutsches Rheuma-Forschungszentrum Berlin	Defining the role of Natural Killer cells in initiating and maintaining autoimmunity	45,000 EUR
Dr. Hedda Wardemann	Max-Planck-Institute Berlin	B cell Self-tolerance and Autoantibodies in Systemic Sclerosis	50,000 EUR
Dr. Jochen Zwerina	University of Erlangen-Nürnberg	The Hemochromatosis Osteoarthritis Registry (THOR)	45,000 EUR

Start-up initiative of the DGRh supports six new research projects since fall 2006

5. IT management

5.1 General aspects of IT-management

The website represents the platform for internal and external communications of the Network. The IT team in Duesseldorf developed applications for rheumatologists and patients, provided and coordinated content and organized its presentation and maintenance until 2006. Thereafter, most of the content was transferred to <http://www.dgrh.de> due to the incorporation of the Network into the DGRh. The responsibility for maintenance and organization of the content was also transferred to DGRh and is now coordinated in the central office.

To facilitate content contributing of all network members and network-wide co-working, the IT team developed an individual dynamic database-driven content management system (CMS) - including various interactive features as a discussion forum, an e-mail answering service, a chat application, a thesaurus and a multimedia archive.

Besides the development of the core CMS, additional applications were integrated into the website:

- ▶ 'Praxis- und Klinikwegweiser' – an online rheumatologists' database for patients
- ▶ 'CME Online Center' – an online e-learning application for continuous medical education (CME) for rheumatologists
- ▶ 'RheumaCheck' – an interactive assessment for rheumatic disorders

These features have been integrated to the new website of the DGRh since the use of this portal for network-wide gathering and preparation of information led to a more effective way of providing and disseminating more reliable, actual, consistent and consented information for patients, physicians and researchers. On the basis of our experiences in website development, we host and administrate websites for other rheumatology-related organisations e.g. the Lupus patient group. These organisations use our CMS and we offer them ongoing IT support.

Another focus was set on the development of the electronic medical documentation system DocuMed.rh. DocuMed is a flexible application for electronic long-term docu-

mentation of patients with rheumatic diseases for research and quality management. The client server, multi-layer software was developed in-house and is implemented in about 50 clinical practices and hospitals. Data interfaces to medical/clinical information systems were established.

The experiences of the development and parts of the code were reused for different online studies and surveys (e.g. LULA study, Mobile Computing study etc.). The IT team developed tools for accessing the collected data for scientific research with statistical analysis software. The IT concept and security policy are in accord with the general guidelines of the Heinrich Heine University of Duesseldorf. The main focus lies on data confidentiality and integrity. Therefore all applications processing and storing sensitive data implement a fine granulated security concept including identity, data access and information rights management components with a role based authorization concept. During the process of software development, different methods of quality management were applied. To keep software flexible and its quality at high level, agile software development methods were adopted, especially the concept of 'Extreme Programming'. This concept includes unit tests, continuous design improvements (refactoring) and a rapid feedback principle.

5.2 Implementation and use of specific IT-management tools

As mentioned above, the IT team developed individual solutions for remote data entry, studies/surveys and telemedicine in-house according to relevant guidelines. DocuMed.rh or its core application was used for medical studies and surveys. Other applications were developed to support medical care (Praxis- und Klinikwegweiser, RheumaCheck, Chat, Email Service) or medical education (CME Online Center). Pseudonymisation tools are still under development in collaboration with 'Telematikplattform für Medizinische Forschungsnetze e.V.' (TMF). Clinical guidelines and quality management programmes are implemented in the design of the content management system and the electronic medical documentation software. The website enabled working groups to develop and revise medical guidelines online (DGRh Guideline early RA).

6. Visibility

6.1 Internet

2003	Topic of the month	
December 2002 January	Psoriatic arthritis	Erlangen
February March	Rational laboratory diagnostics	Freiburg
April May	Sjögren-Syndrom	Hannover
June July	Vaccination under immunosuppression	Lübeck
August September	Early rheumatoid arthritis	Düsseldorf
October - December	New therapies for rheumatoid arthritis	Berlin

2004	Topic of the month	
January February	Hypertension	Erlangen
March April	Systemic sclerosis	Freiburg
May June	Giant cell arteriitis	Hannover
July August	New therapies for systemic vasculitides	Lübeck
September - November	New rheumatic factor: CCP-antibody	Düsseldorf
December - March 2005	Early rheumatoid arthritis (diagnosis, prognosis, therapy)	Berlin

2005	Topic of the month	
December 2004 - March	Early rheumatoid arthritis (diagnosis, prognosis, therapy)	Berlin
April - June	Non-infectuous myositis	Freiburg
July August	Lyme disease	Hannover
September October	Diagnosis of systemic vasculitides	Lübeck
November December	Smoking and rheumatoid arthritis	Düsseldorf

2006	Topic of the month	
January February	Stem cells transplantation with SLE	Berlin
March April	Vaccination for children with rheumatic diseases	Berlin
May June	Immune system	Jena
July August	Pain therapy	Leipzig
Oktober November	Early diagnosis of spondylitis ankylosans	Berlin
Dezember January	Chondral replacement and artificial joints	Hamburg

The establishment of our internet platform www.rheumanet.org has been a successful communication tool both for members within the network as well as for doctors, patients and other parties interested in the field of rheumatology. With the integration of the network into the German Society of Rheumatology DGRh it became necessary to build a common communication platform. In consequence the websites of www.rheumanet.org and www.dgrh.de were merged to one site and launched at the annual congress in Wiesbaden in 2006. This relaunch was used to modernise the design as well as the features which

support several functions. An internal member's areas now allows direct access to all protocols and documents of different active groups and allows a maximum of transparency. Especially the research section represents the activities of the Competence Network. Here, we established a research data base where all active groups can sign up and give information on their main research focus, material banks, cohorts, publications, grants etc. This research data base is an excellent tool to search for cooperation partners, biomaterial and to get a quick overview of the different activities in the groups.

6. Visibility

Since the launch in October 2006 the content is permanently updated and extended. In 2007 a new section especially for patients has been developed. An interactive map with all Regional Cooperative Arthritis Centres in Germany helps to find doctors in special areas. A campaign to promote the 'Early diagnosis of inflammatory rheumatic diseases' has been in the focus in 2007 and peaks on the World Arthritis Day on 12th of October. This campaign is backed up by detailed information for doctors as well as for patients. Results from projects of the Competence Network like the evidence-based guideline for early RA or the recommendations for early diagnosis of SpA from the GESPIC cohort are translated here to a broad audience.

One of the most successful online activities is the 'topic of the month' which started at the beginning of the Network and is continued with new articles every other month, addressed to either GPs or to patients. The six Network centres are responsible for providing the content once a year. The authors host the internet expert chat on two successive evenings. In September/October e.g. the topic of the month is the 'early recognition of arthritis ankylosans' in accordance to the above mentioned campaign and World Arthritis Day. The list shows the complete issues from 2004 to 2007. All activities regarding the internet platform are now coordinated in the central office in Berlin.

6.2 Public relations activities

Activity	2003	2004	2005	2006	Multipier
Press conferences	2	4	3	3	supraregional
Press releases	9	14	11	9	supraregional
Reports by news agencies	117	5	13	20	supraregional
Public press reports	41	30	50	299	general public
Scientific/medical press	25	17	38	70	supraregional
Online/Internet reports	60	23	63	46	general public
TV/Radio presentations	9	7	10	18	general public

Number of press activities from 2003 – 2006. In 2006 the numbers reflect the joint activities of the Network and the DGRh. All press releases are listed on the DGRh homepage (www.dgrh.de).

6.3 Presentations at scientific conferences

	2003	2004	2005	2006
Congresses national	57	34	42	24
Congresses international	18	48	18	31

Number of presentations at national and international conferences from BMBF-funded projects. Details of abstracts are listed in Annex.

7. Sustainability

The competence network has been successfully integrated as a self-contained section (Arbeitsgemeinschaft, AG) into the DGRh. As an AG the Network is aiming at coordinating and fostering excellent research in the field, following also the ideas of the current 'Roadmap' of the German Ministry of Health. To keep up excellent research in the Network all members need to have reviewed projects and an active contribution to the Network's activities. The focus is no longer on inflammatory diseases only but includes now also the field of osteoarthritis and osteoimmunology.

Many steps have been already taken to maintain the activities in the long run by the acquisition of various sources of financing:

- ▶ The DGRh has given grants for start-up research projects (300.000 Euro) and for travel fellowships.
- ▶ The Collaborative Arthritis Centers support transfer projects and the national database every year with 50.000 Euro.
- ▶ The deans of the medical facilities of the six competence centers have agreed to continue the funding from 2008 onwards based on a positive final evaluation of the network by the scientific advisory board.
- ▶ The scientific meetings such as the 'Forum of experimental rheumatology' and the 'VISION workshop' are integrated in the annual DGRh congress and costs will be covered by the congress profits.
- ▶ The industry forum is financing basic costs of the central office by membership fees and supports the national database starting in 2007 with an extensive programme (200.000 Euro in total).
- ▶ EU projects have already supported research coordination and European networking activities that will hopefully lead to even more successful grant applications in the future.

- ▶ The DGRh will finance the central coordinator of the competence network, the research coordinator position for an interim time period until EU funding is available, half a position for internet support as well as some funding for press activities. With this support all major activities in the central office can be continued after the BMBF funding period.

The major focus is now to establish a charity for rheumatology research. Fundraising is a potential source of income as charities in other countries such as the Netherlands, United Kingdom and the USA are successfully demonstrating. The DGRh has decided to set a budget of 100.000 Euro aside to build up fundraising activities. During the course of this year several meetings with the patient organization Rheuma-Liga have led to a concept where both organizations want to set up a common arthritis foundation with the aim to raise money for research activities in this field. A detailed concept has been worked out by the central coordinator which is momentarily under revision and should be accepted in fall by both of the general member meetings.









Considering all the preparations the official start of the fundraising activities is aimed for the beginning of 2008. In order to be successful with fundraising the tasks for this project include a variety of features such as setting up a valid database, producing information material, organizing events, educating rheumatologists, fostering international exchange, involving volunteers and running campaigns. This can be only performed by engaging a professional fundraiser who will have the support of the central office facilities and public relations. It will take at least three years until a substantial amount of money will be available for research funding and both DGRh and Rheuma-Liga have committed themselves to support the fundraising activities now and from 2008 onwards.

In summary, the network has initiated all crucial steps for a sustained structure after the 3rd funding period. The integration in the DGRh secures the Network on a national level; the various EU activities on an international level. The involvement of the industry forum will secure the basic finances with expected increase over the years and a successful fundraising should raise substantially amounts of funds for research projects in the long run.






Annex

Publications 2003

- Brandt J, Khariouzov A, Listing J, Haibel H, Sorensen H, Grassnickel L, Rudwaleit M, Sieper J, Braun J. Six-month results of a double-blind, placebo-controlled trial of etanercept treatment in patients with active ankylosing spondylitis. *Arthritis Rheum* 2003; 48:1667-75.
- Brandt J, Westhoff G, Rudwaleit M, Listing J, Zink A, Braun J, Sieper J. Validierung einer deutschen Version des Fragebogens BASDAI zur Messung der Krankheitsaktivität bei ankylosierender Spondylitis. *Z Rheumatol* 2003; 62: 264-273.
- Braun J, Baraliakos X, Golder W, Brandt J, Rudwaleit M, Listing J, Bollow M, Sieper J, van der Heijde D: MRI imaging examinations of the spine in patients with ankylosing spondylitis, before and after successful therapy with Infliximab. *Arthritis Rheum* 48:1126-1136, 2003.
- Dorner, B.G., S. Steinbach, M.B. Huser, R.A. Kroczeck, and A. Scheffold. 2003. Single-cell analysis of the murine chemokines MIP-1alpha, MIP-1beta, RANTES and ATAC/lymphotactin by flow cytometry. *J Immunol Methods* 274:83-91.
- Egerer K, Hertzler J, Feist E, Albrecht A, Rudolph PE, Dorner T, Burmester GR. sE-selectin for stratifying outcome in rheumatoid arthritis. *Arthritis Rheum*. 2003 Aug 15; 49(4):546-8.
- Franz J, Krause A: Lyme disease (Lyme borreliosis). *Baillière's Best Practice and Research in Clinical Rheumatology* 17:241-264, 2003
- Huppertz HI, Krause A: Lyme-Borreliose. *Internist* 44:175-183, 2003
- Jayne D, Rasmussen N, Andrassy K, Bacon P, Tervaert JW, Dadonienė J, Ekstrand A, Gaskin G, Gregorini G, de Groot K, Gross W, Hagen EC, Mirapeix E, Pettersson E, Siegert C, Sinico A, Tesar V, Westman K, Pusey C; European Vasculitis Study Group. A randomised trial of maintenance therapy for vasculitis associated with antineutrophil cytoplasmic autoantibodies. *N Engl J Med*. 2003 Jul 3; 349(1):36-44.
- Jendro, M.C., Fingerle, F., Deutsch, T., Liese, A., Köhler, L., Kuipers, J.G., Raum, E., Martin, M., Zeidler, H. Chlamydia trachomatis-infected monocytes induce apoptosis of activated T cells by secretion of tumor-necrosis-factor-alpha in vitro. *Med. Microbiol. Immunol* 2003
- Kary S, Burmester GR, Buttgerit F. Pharmakotherapie rheumatischer Erkrankungen im Alter. *Internist* 2003 Aug; 44(8):951-8.
- Kary S, Burmester GR. Anakinra: The first interleukin-1 inhibitor in the treatment of rheumatoid arthritis. *Int J Clin Pract*. 2003 Apr; 57(3):231-4. Review.
- Kruetzmann S, Rosado MM, Weber H, Germing U, Tournilhac O, Peter HH, Berner R, Peters A, Boehm T, Plebani A, Quinti I, Carsetti R: Human immunoglobulin M memory B cells controlling *Streptococcus pneumoniae* infections are generated in the spleen. *J Exp Med*, 2003; 197 (7):939-945
- Kuipers, J.G., Zeidler, H., Köhler, L. How does Chlamydia cause arthritis? *Rheum Dis Clin N America* 2003, 29: 613-629
- Lindenau S, Scholze S, Odendahl M, Dörner T, Radbruch A, Burmester G-R & Berek C (2003) Aberrant activation of B cells in patients with rheumatoid Arthritis. *Ann. N. Y. Acad. Sci.* 987:246-248
- Lünemann JD, Krause A. Heterogenität von *Borrelia burgdorferi*: Ätiopathogenetische Relevanz und klinische Implikationen. *Z Rheumatol* 62:148-154, 2003
- Minden K, Schöntube M. Häufigkeit und Prognose rheumatischer Erkrankungen im Kindesalter. *rheuma aktuell* 2002; 1: 32-35.
- Mittendorf T, Merkesdal S, Huelsemann JL, Schulenburg JM, Zeidler H, Ruof J. Implementing standardized cost categories within economic evaluations in musculoskeletal diseases. *Eur J Health Econ* 2003; 4(i):43-9
- Priem S, Munkelt K, Franz JK, Schneider U, Werner T, Burmester GR, Krause A: Epidemiologie und Therapie der Lyme-Arthritis und anderer Manifestationen der Lyme-Borreliose in Deutschland: Ergebnisse einer bundesweiten ärzteumfrage. *Z Rheumatol* 62:450-458, 2003
- Reichel, P.H., C. Seemann, E. Csernok, J.M. Schröder, A. Müller, W.L. Gross, H. Schultz, The bactericidal/permeability increasing protein is expressed by human dermal fibroblasts and upregulated by IL-4, *Clin Diagn Lab Immunol* 2003; 10(3):473-475
- Reinhold-Keller E, Fink CO, Herlyn K, Gross WL, De Groot K. High rate of renal relapse in 71 patients with Wegener's granulomatosis under maintenance of remission with low-dose methotrexate. *Arthritis Rheum* 2002; 47:(3):326-32.
- Richter J, Becker A, Specker Ch, (2003) Rheumatologische Informationen im Internet – Erfahrungen aus dem Projekt RheumaNet des Rheumazentrums Düsseldorf, *Z Rheumatol*. 2003 Aug; 62(4):395-401.
- Richter J, Specker Ch, Becker A, Monser R, Arendt D, Knop J, Schneider M (2003) Beitrag des Internet zur Qualitätssicherung in der Rheumatologie. *Z Arztl Fortbild Qualitätssich* 97:365-376.

-  Ruof J, Huelsemann JL, Mittendorf T, Handelmann S, von der Schulenburg JM, Zeidler H, Merkesdal S. Costs of Rheumatoid Arthritis in Germany. A micro-costing approach based on objective data source *Ann Rheum Dis* 2003 Jun; 62(6): 544-9
-  Scheel AK, Netz JU, Hermann KG, Hielscher AH, Klose AD, Tresp V, Schwaighofer A, Müller GA, Burmester GR, Backhaus M: Laser imaging techniques for follow-up analysis of joint inflammation in patients with rheumatoid arthritis. *Medical Laser Appl* 2003, 18: 198-206
- Schulze-Koops, H. and J. R. Kalden. 2003. Targeting T cells in rheumatic diseases. In: *Biological Therapy in Rheumatology*, edited by J. S. Smolen and by P. E. Lipsky. Martin Dunitz Publishers, London: Chapter 1, pp 3-24
-  Schwinzer R, Witte T, Hundrieser J, Ehlers S, Momot T, Hunzelmann N, Krieg T, Schmidt RE, Wonigeit K. Enhanced frequency of a PTPRC (CD45) exon A mutation (77C-->G) in systemic sclerosis. *Genes Immun* 2003; 4:168-9.
-  Witte T, T Matthias, M Oppermann, K Helmke, HH Peter, RE Schmidt, M Tishler. Prevalence of Antibodies against Alpha-Fodrin in Sjögren's syndrome: Comparison of two Sets of Classification Criteria. *J Rheumatol* 2003; 30:2157-9.
- Ulbricht, KU, RE Schmidt, T Witte. Antibodies against alpha-fodrin in Sjögren's syndrome. *Autoimmunity Reviews* 2003; 2:109-113.
-  Wagner U, Kaltenhäuser S, Pierer M, Seidel W, Tröltzsch M, Häntzschel H, Kalden JR, Wassmuth R: Prospective analysis of the impact of HLA-DR and -DQ on joint destruction in recent-onset rheumatoid arthritis, *Rheumatology* 42 (2003) 553-562.
-  Wagner, UG, Pierer, M, Kaltenhaeuser, S, Wilke, B, Arnold, S, Haentzschel, H.: Clonally expanded CD4+CD28 null T cells in RA use distinct combinations of T cell receptor BV and BJ elements. *Eur J Immunol*, 2003 Jan; 33(1):79-84.
- Warnatz K, Peter HH, Schumacher M, Wiese L, Prasse A, Petschner F, Vaith P, Volk B, Weiner SM: Infectious CNS disease as a differential diagnosis in systemic rheumatic diseases: three case reports and a review of the literature *Ann Rheum Dis*, 2003; 62: 50-57
-  Westhoff G, Weber C, Zink A. Noch zu selten diagnostiziert: Osteoporose bei Patienten mit früher rheumatoider Arthritis. *MedReport* 2003; 27 (9): 11.
-  Zink A, Huscher D, Listing J. Die Kerndokumentation der Regionalen Kooperativen Rheumazentren als Instrument der klinischen Epidemiologie und der Qualitätssicherung der rheumatologischen Versorgung. *Z Arztl Fortbild Qualitätssich* (2003) 97: 399-405.
- Zou J, Rudwaleit M, Brandt J, Thiel A, Braun J, Sieper J. Down-regulation of the nonspecific and antigen-specific T cell cytokine response in ankylosing spondylitis during treatment with infliximab. *Arthritis Rheum* 2003; 48(3):780-90.
- Zou J, Rudwaleit M, Brandt J, Thiel A, Braun J, Sieper J. Up regulation of the production of tumour necrosis factor alpha and interferon gamma by T cells in ankylosing spondylitis during treatment with etanercept. *Ann Rheum Dis* 2003; 62(6):561-4.
- Zou J, Zhang Y, Thiel A, Rudwaleit M, Shi SL, Radbruch A, Poole R, Braun J, Sieper J. Predominant cellular immune response to the cartilage autoantigenic G1 aggrecan in ankylosing spondylitis and rheumatoid arthritis. *Rheumatology (Oxford)* 2003; 42(7):846-55. Epub 2003 Feb 28.

Publications 2004

- Bartholome B., C.M. Spies, T. Gaber, S. Schuchmann, T. Berki, D. Kunkel, M. Bienert, A. Radbruch, G.R. Burmester, R. Lauster, A. Scheffold, and F. Buttgereit. 2004. Membrane glucocorticoid receptors (mGCR) are expressed in normal human peripheral blood mononuclear cells and up-regulated after in vitro stimulation and in patients with rheumatoid arthritis. *Faseb J* 18:70-80.
- Brandt J, Khariouzov A, Listing J, Haibel H, Sorensen H, Rudwaleit M et al. Successful short term treatment of patients with severe undifferentiated spondyloarthritis with the anti-tumor necrosis factor-alpha fusion receptor protein etanercept. *Journal of Rheumatology* 2004; 31(3):531-538.
- Burmester GR, Kamradt T, Krause A: Lyme disease. In: Isenberg DA, Maddison PJ, Woo P, Glass D, Breedveld FC (ed.): *Oxford Textbook of Rheumatology*: 613-620, 2004
-  Csernok E, Stellenwert der Antineutrophilen zytoplasmatischen Antikörper (ANCA) in der Diagnostik von Vaskulitiden, *Med Welt* 2004; 55:78-84
- Csernok E., Anti-neutrophil cytoplasmic antibodies and pathogenesis of small vessel vasculitides. *Autoimmun Rev.* 2003 May; 2(3):158-64.
-  Csernok, E., Holle, J., Cohen-Tervaert, J. W., Westmann, K., Wieslander, J., Niles, J. L., Kallenberg, C.G., Specks, U. (2004). Capture ELISA is more sensitive than direct ELISA for detection of antineutrophil cytoplasmic antibodies directed against proteinase 3 in Wegener's granulomatosis: first results from a multicenter study. *Rheumatology (Oxford)*. 43(2):174-80.
-  De la Rosa, M., Rutz, S. Dorninger H. and A. Scheffold. 2004. Interleukin-2 is essential for CD4⁺CD25⁺ regulatory T cell function. *Eur J Immunol* 34(9):2480-8.
- Dorner T, Egerer K, Feist E, Burmester GR. Rheumatoid factor revisited. *Curr Opin Rheumatol.* 2004 May; 16(3):246-53.
- F. Dodeller, A. Skapenko, J.R. Kalden, and H. Schulze-Koops. 2004. The p38 MAP kinase specifically controls Th2 effector functions in human CD4 T cells. *Clin. Invest. Med.* 27:141A
- Drynda S, Ringel B, Kekow M, Kuhne C, Drynda A, Glocker MO, Thiesen HJ, Kekow J., Proteome analysis reveals disease-associated marker proteins to differentiate RA patients from other inflammatory joint diseases with the potential to monitor anti-TNFalpha therapy. *Pathol Res Pract.* 2004; 200(2):165-71.
- Farge D, Passweg J, van Laar JM, Marjanovic Z, Besenthal C, Finke J, Peter HH, Breedveld FC, Fibbe WE, Black C, Denton C, Koetter I, Locatelli F, Martini A, Schattenberg AV, van den Hoogen F, van de Putte L, Lanza F, Arnold R, Bacon PA, Bingham S, Ciceri F, Didier B, Diez-Martin JL, Emery P, Feremans W, Hertenstein B, Hiepe F, Luosujarvi R, Leon Lara A, Marmont A, Martinez AM, Pascual Cascon H, Bocelli-Tyndall C, Gluckman E, Gratwohl A, Tyndall A; EBMT/EULAR Registry. Autologous stem cell transplantation in the treatment of systemic sclerosis: report from the EBMT/EULAR Registry. *Ann Rheum Dis.* 2004 Aug; 63(8):974-81.
- Haibel H, Niewerth M, Brandt J, Rudwaleit M, Listing J, Sieper J et al. Measurement of quality of life in patients with active ankylosing spondylitis being treated with infliximab-a comparison of SF-36 and SF-12. *Z Rheumatol* 2004; 63(5):393-401.
- Haibel H, Rudwaleit M, Sieper J, Zeidler H, Kuipers JG. Diagnose der reaktiven Arthritis. *Z Rheumatol* 2004;63:211-5.
-  Hielscher AH, Klose A, Scheel AK, Moa-Anderson B, Backhaus M, Netz U, Beuthan J: Sagittal Laser Optical Tomography for Imaging of Rheumatoid Finger Joints. *Physics in Medicine and Biology* 49(7), 1147-1163 (2004)
-  Huehn, J., K. Siegmund, J.C. Lehmann, C. Siewert, U. Haubold, M. Feuerer, G.F. Debes, J. Lauber, O. Frey, G.K. Przybylski, U. Niesner, M. De La Rosa, C.A. Schmidt, R. Brauer, J. Buer, A. Scheffold, and A. Hamann. 2004. Developmental Stage, Phenotype, and Migration Distinguish Naive- and Effector/Memory-like CD4⁺ Regulatory T Cells. *J Exp Med* 199:303-313.
- Kuon W, Kuhne M, Busch DH, Atagunduz P, Seipel M, Wu P, Morawietz L, Fernahl G, Appel H, Weiss EH, Krenn V, Sieper J. Identification of novel human aggrecan T cell epitopes in HLA-B27 transgenic mice associated with spondyloarthropathy. *J Immunol.* 2004 Oct 15;173(8):4859-66.
- Prots I., A. Skapenko, S. Mattyasovszky, C. L. Yoné, J. R. Kalden, and H. Schulze-Koops. 2004. Regulation of T cell differentiation by IL-4R a-chain single nucleotide polymorphisms. *Arthritis Res. Ther.* 6:S3/28
- Prots I., S. Mattyasovszky, C. L. Yoné, J. R. Kalden, H. Schulze-Koops, and A. Skapenko. 2004. Regulation of T cell differentiation by IL-4R alpha chain single nucleotide polymorphisms. *Ann. Rheum. Dis.* 63:S1/124
- Isaacs JD, Thiel A. Stem cell transplantation for autoimmune disorders. Immune reconstitution. *Best Pract Res Clin Haematol.* 2004; 17:345-358.

- Jagiello P, M Gencik, L Arning, S Wiczorek, E Kunstmann, E Csernok, WL Gross, JT Epplen. New genomic region for Wegener's granulomatosis as revealed by an extended association screen with 202 apoptosis related genes. *Hum Genet* 114:468-477, 2004
- Jendro, M.C., F. Fingerle, T. Deutsch, A. Liese, L. Köhler, J.G. Kuipers, E. Raum, M. Martin, H. Zeidler. Chlamydia-trachomatis-infected macrophages induce apoptosis of activated T cells by secretion of Tumor-Necrosis-factor alpha in vitro. *Med. Microbiol. Immunol.* 193: 45-52, 2004.
- Korn JH, Mayes M, Matucci Cerinic M, Rainisio M, Pope J, Hachulla E, Rich E, Carpentier P, Molitor J, Seibold JR, Hsu V, Guillevin L, Chatterjee S, Peter HH, Coppock J, Herrick A, Merkel PA, Simms R, Denton CP, Furst D, Nguyen N, Gaitonde M, Black C..Digital ulcers in systemic sclerosis: prevention by treatment with bosentan, an oral endothelin receptor antagonist. *Arthritis Rheum.* 2004 Dec; 50(12):3985-93.
- Krauß-Opatz, B., C. Schmidt, A. Bialowons, U. Fendrich, V. Kaefer, H. Zeidler, J. Kuipers, L. Köhler. Production of PGE₂ in monocytes infected in vitro with Chlamydia trachomatis and Chlamydia pneumoniae. *Microbial Pathogenesis* 37: 155-161, 2004.
- Leipe, Jan, Alla Skapenko, Uwe Niesner, Koen Devriendt, Rolf Beetz, Andreas Radbruch, Joachim R. Kalden, Peter E. Lipsky, and Hendrik Schulze-Koops. GATA-3 in human Th2 development. *J Exp Med.* 2004 Feb 2; 199(3):423-8.
- Liang MH, P Fortin, M Schneider, M Abrahamowicz et al., ACR Ad Hoc Committee on SLE Response Criteria. Steroid Sparing Ability of Interventions in Systemic Lupus Erythematosus. *Arthritis Rheum*, 50: 3427-3431
- Liang MH, P Fortin, M Schneider, M Abrahamowicz et al., ACR Ad Hoc Committee on SLE Response Criteria. The American College of Rheumatology Response Criteria for Systemic Lupus Erythematosus Clinical Trials: Overall Disease Activity. *Arthritis Rheum* 50: 3418-26.
- Masilamani M, Nowack R, Witte T, Schlesier M, Warnatz K, Glocker MO, Peter HH, Illges H. Reduction of soluble complement receptor 2/CD21 in systemic lupus erythematosus and Sjogren's syndrome but not juvenile arthritis. *Scand J Immunol.* 2004 Dec; 60(6):625-30.
- Metzler C, Fink C, Lamprecht P, Gross WL, Reinhold-Keller E., Maintenance of remission with leflunomide in Wegener's granulomatosis. *Rheumatology (Oxford).* 2004 Mar; 43(3):315-20.
- Meyer P, Özkan V, Holtgrave E A, Freesmeyer W, Minden K, Niewerth M. TMJ Disorders in juvenile idiopathic arthritis. *J Dent Res* 83[Spec Iss B], 0293. 2004.
- Minden K, Niewerth M, Möbius D, Ganser G, Küster R-M, Zink A und AGKJR. Rheumatologische Versorgung Jugendlicher und junger Erwachsener mit juveniler Arthritis. *Z Rheumatol* 2004; 63:3; 266.
- Minden K, Niewerth M, Zink A und Kinderrheumatologen der AG Kinder- und Jugendrheumatologie. 2004. Kerndokumentation rheumakrankter Kinder und Jugendlicher. *Arthritis Rheum* 2004; 24; 69-73.
- Minden K, Niewerth M, Zink A und Kinderrheumatologen der AG Kinder- und Jugendrheumatologie. Kerndokumentation rheumakrankter Kinder und Jugendlicher. *Med Welt* 2004; 55; 73-77.
- Minden K, Niewerth M, Zink A, Schneider M. Prognose des systemischen Lupus erythematosus. *Z Rheumatol* 2004; 63:3; 264.
- Minden K, Niewerth M, Zink A. Prognose rheumakrankter Kinder. *Pädiatrie hautnah* 2004; S1:S21.
- Minden, K, Niewerth, M, Listing J, Biedermann T, Schöntube M, Zink A. Burden and cost of illness in adult patients with juvenile idiopathic arthritis. *Ann Rheum Dis* 2004; 63:7; 836-42.
- Niewerth M, Minden K, Ganser G, Küster RM, Möbius D, Zink A. Therapiecompliance bei rheumakranken Kindern und Jugendlichen. *Gesundheitswesen* 2004; 66:119
- Niewerth M, Minden K, Möbius D, Ganser G, Küster R-M, Zink A und AGKJR. Die juvenile idiopathische Arthritis beim Übergang ins Erwachsenenalter. *Z Rheumatol* 2004; 63:3; 267.
- Radbruch A, Steinkötter J, Thiel A. Neue kurative Immuntherapien für entzündliche-rheumatische Autoimmunerkrankungen. *Med Welt* 2004; 55:67-72
- Reiners, K., Hansen, P.H., Krüssmann, A. Schön, Gisela, Stöcker, M., Csernok, E, Gross, W.L., Engert, A., Pogge von Strandmann, E. Selective killing of B-cell hybridomas targeting proteinase 3, Wegener's autoantigen. *Immunology.* 2004 Jun; 112(2):228-36.
- Richter J, Becker A, Specker Ch, Monser R, Schneider M (2004) Krankheitsbezogene Internetnutzung bei Patienten mit entzündlich-rheumatischen Systemerkrankungen. *Z Rheumatol.* 63:216-22.
- Rihl M, Baeten D, Seta N, Gu J, Filip De Keyser F, Veys EM, Kuipers JG, Zeidler H, Yu DTY. Technical Validation of cDNA-Based microarray as screening technique to identify candidate genes in synovial tissue biopsies from Spondyloarthritis patients, *Ann Rheum Dis* 2004, May; 63(5) 498-508

- Rihl M, Gu J, Baeten D, Marker-Hermann E, Goodall JC, Gaston JS, Kuipers JG, Zeidler H, Yu DT. Alpha beta but not gamma delta T cell clones in synovial fluids of patients with reactive arthritis show active transcription of tumour necrosis factor alpha and interferon gamma. *Ann Rheum Dis.* 2004 ; 63(12):1673-6.
- Rudwaleit M, Listing J, Brandt J, Braun J, Sieper J. Prediction of a major clinical response (BASDAI 50) to tumour necrosis factor alpha blockers in ankylosing spondylitis. *Ann Rheum Dis* 2004; 63:665-70.
- Rudwaleit M, Sieper J. Diagnose und Frühdiagnose der ankylosierenden Spondylitis. *Z Rheumatol* 2004; 63:193-202.
- Rufenach C, Burmester GR, Zeidler H, Radbruch A. Kompetenznetz Entzündliche-rheumatische Erkrankungen. *Internist* 2004; 45:409-14
- Rufenach C. Kompetenznetz Rheuma optimiert Patientenversorgung auf allen Ebenen. *Rheumaplast* 2004; BAND(7):26-7
- Rutz, S., and A. Scheffold. 2004. Towards in vivo application of RNA interference: new toys, old problems. *Arthritis Research & Therapy* 6(2):78-85.
- Ruof J, Huelsemann JL, Mittendorf T, Handelsmann S, Aultman R, von der Schulenburg JM, Zeidler H, Merkesdal S. Comparison of estimated medical costs among patients who are defined as having rheumatoid arthritis using three different standards. *Eur J Health Econ.* 2004 Feb; 5(1):64-9.
- Schmitt, A., D. Schubert, C. Sengler, and T. Kamradt. 2004. Autoantibodies against Glucose-6-phosphate-isomerase are not a diagnostic marker for juvenile idiopathic arthritis. *Ann Rheum Dis* 63:463.
- Schotte H, Schluter B, Drynda S, Willeke P, Tidow N, Assmann G, Domschke W, Kekow J, Gaubitz M. Abstract Interleukin 10 promoter microsatellite polymorphisms are associated with response to long term treatment with etanercept in patients with rheumatoid arthritis. *Ann Rheum Dis.* 2005 Apr; 64(4):575-81. Epub 2004 Sep 2.
- Schubert, D., B. Maier, L. Morawietz, V. Krenn, and T. Kamradt. 2004. Immunization with glucose-6-phosphate isomerase induces T-cell dependent peripheral polyarthritis in genetically unaltered mice. *J. Immunol.* 172:4503-4509.
- Thiel A, Scheffold A, Radbruch A. (2004) Antigen-specific cytometry-new tools arrived! *Clin Immunol.* 111(2):155-61.
- Ullrich S; Schumacher U; Ai MX; Gay S; Schechner JS; Pober JS; Gross WL and Csernok E; Transfer of human leukocytes into double knock out Pfp^{-/-}Rag2^{-/-} mice grafted with human skin: increased accumulation of neutrophils in the human dermal microvessels. *Transplantation.* 2004 Nov 27; 78(10):1557-9.
- von Mikecz, Hemmerich P; *Subnuclear Pathology. Visions of the Cell Nucleus, 2004* by American Scientific Publishers.
- Wagner U., Pierer M., Wahle M., Moritz F., Kaltenhäuser S., Häntzschel H. Ex vivo homeostatic proliferation of CD4+ T cells in rheumatoid arthritis is dysregulated and driven by membrane-anchored TNFα. 2004. *J Immunol* 173:2825-33
- Wehr C, Eibel H, Masilamani M, Illges H, Schlesier M, Peter HH, Warnatz K. : A new CD21low B cell population in the peripheral blood of patients with SLE. *Clin Immunol.* 2004 Nov; 113(2): 161-71
- Weiner SM, Thiel J, Berg T, Weber S, Krumme B, Peter HH, Rump LC, Groth WH. Impact of in vivo complement activation and cryoglobulins on graft outcome of HCV- infected renal allograft recipients. *Clin Transplant* 2004;18:7-13
- Westhoff G, Listing J, Zink A. Was kostet die rheumatoide Arthritis den Erkrankten? Out-of-Pocket-Ausgaben im Frühstadium der Erkrankung. *Z Rheumatol* 2004; 63(5):414-424.
- Zeidler, H., J.G. Kuipers, L. Köhler. Chlamydia-induced arthritis. *Curr. Op. Rheumatol.* 16: 380-392, 2004.
- Zink A, Fischer-Betz R, Thiele K, Listing J, Huscher D, Gromnica-Ihle E et al. Health care and burden of illness in systemic lupus erythematosus compared to rheumatoid arthritis: results from the national database of the German Collaborative Arthritis Centres. *Lupus* 2004; 13(7):529-536.
- Zink A, Huscher D, Thiele K, Listing J, Schneider M. Die Kerndokumentation der Rheumazentren. Ein Instrument der evaluativen Versorgungsforschung. 12. Bundesgesundhbl-Gesundheitsforsch-Gesundheitsschutz 2004; 47(6):526-532.
- Zink A, Huscher D. Longterm Studies in Rheumatoid Arthritis - The German Experience. *J Rheumatol* 2004; 31(Suppl. 69):22-26.
- Zink A. Methodische Aspekte der Gesundheitsökonomie. *Z Rheumatol* 2004; 63(5):369-371.


Publications 2005

- Akkad D, Jagiello P, Szyld P, Goedde R, Wiczorek S, Gross WL, Epplen J (2005) Promoter polymorphism rs3087456 in the MHC class II transactivator gene is not associated with susceptibility for selected autoimmune diseases in German patient groups. *Int J Immunogenet* 33:59-61.
- Baraliakos X, Brandt J, Listing J, Haibel H, Sorensen H, Rudwaleit M, Sieper J, Braun J. Outcome of patients with active ankylosing spondylitis after two years of therapy with etanercept: clinical and magnetic resonance imaging data. *Arthritis Rheum.* 2005 Dec 15;53(6):856-63. 31:
- Baraliakos X, Listing J, Brandt J, Zink A, Alten R, Burmester G, Gromnica-Ihle E, Kellner H, Schneider M, Sorensen H, Zeidler H, Rudwaleit M, Sieper J, Braun J. Clinical response to discontinuation of anti-TNF therapy in patients with ankylosing spondylitis after 3 years of continuous treatment with infliximab. *Arthritis Res Ther.* 2005; 7(3):R439-44.
- Baraliakos X., J. Listing, J. Brandt, M. Rudwaleit, J. Sieper, J. Braun. Progression of radiographic damage in patients with as – assessment of definite change and definition of predictive factors. *Ann Rheum Dis* 2005;64 (Suppl III):335
- Bley TA, Warnatz K, Wieben O, Uhl M, Scholz C., Vaith P, Peter HH, Langer M High-resolution MRI in giant cell arteritis with multiple inflammatory stenosis. *Rheumatology (Oxford).* 2005 Apr 19.
- Bockermann R, Schubert D, Kamradt T, Holmdahl R. Induction of a B-cell-dependent chronic arthritis with glucose-6-phosphate isomerase. *Arthritis Res Ther.* 2005;7(6):R1316-24. Epub 2005 Sep 20.
- Brandt H.C., H. Haibel, S. Zinke, I. Spiller, M. Rudwaleit, J. Sieper. Performance Of Early Recommendations For Axial Spondyloarthritis In Patients With Chronic Back Pain. *Ann Rheum Dis* 2005;64(Suppl III):331
- Brandt J, Listing J, Haibel H, Sorensen H, Schwebig A, Rudwaleit M, Sieper J, Braun J. Long-term efficacy and safety of etanercept after readministration in patients with active ankylosing spondylitis. *Rheumatology (Oxford).* 2005 Mar; 44(3):342-8
- Burkhardt H, Sehnert B, Bockermann R, Engstrom A, Kalden JR, Holmdahl R. Humoral immune response to citrullinated collagen type II determinants in early rheumatoid arthritis. *Eur J Immunol.*; 35: 1643-52 (2005)
- Chen M, Dittmann A, Kuhn A, Ruzicka T, von Mikecz A. Recruitment of topoisomerase I (Scl-70) to nucleoplasmic proteasomes in response to xenobiotics suggests a role for altered antigen processing in scleroderma. *Arthritis Rheum.* 2005 Mar; 52(3):877-884
- Chen M, von Mikecz A. Proteasomal processing of nuclear autoantigens in systemic autoimmunity. *Autoimmun Rev.* 2005 Mar; 4(3):117-122
- Chen M, von Mikecz A. Xenobiotic-induced recruitment of autoantigens to nuclear proteasomes suggests a role for altered antigen processing in Scleroderma. *Ann. N.Y. Acad. Sci.*, 2005
- Detert J, Burmester GR. *Medical Tribune* 3, 2005. Frühe rheumatoide Arthritis.
- Dinser R., M. C. Jendro, S. Schnarr, H. Zeidler. Antibiotic treatment of Lyme - Borreliosis: What is the evidence? *Ann. Rheum. Dis.* 2005, 64: 519-523.
- Feldtkeller E, Rudwaleit M, Sieper J. Erleichterte Bestimmung der befundabhängigen Wahrscheinlichkeit einer ankylosierenden Spondylitis. *Z Rheumatol* 2005; 64(suppl 1):I/84
- Frey O, Petrow PK, Gajda M, Siegmund K, Huehn J, Scheffold A, Hamann A, Radbruch A, Brauer R. The role of regulatory T cells in antigen-induced arthritis: aggravation of arthritis after depletion and amelioration after transfer of CD4+CD25+ T cells. *Arthritis Res Ther.* 2005; 7(2):R291-301
- Grützkau A., J. Steinkötter; Kompetenzzentrum für die Rheumaforschung, Deutsche Zeitschrift für Klinische Forschung 1/2-2005
- Haibel H, Brandt HC, Rudwaleit M, Sieper J. Offene Pilotstudie mit Methotrexat 20mg bei Patienten mit aktiver ankylosierender Spondylitis. *Z Rheumatol* 2005; 64(suppl 1):I/84
- Haibel H, Rudwaleit M, Braun J, Sieper J. Six months open label trial of leflunomide in active ankylosing spondylitis. *Ann Rheum Dis.* 2005 Jan; 64(1):124-6.
- Heiligenhaus A, Niewerth M, Mingels A, Ganser G, Thon A, Pleyer U, Greiner K, Minden K. Epidemiologische Daten zur Uveitis bei juveniler idiopathischer Arthritis aus einer bundesweiten pädiatrischen und ophthalmologischen Datenerhebung (Uveitis-Modul der Kerndokumentation). *Klinische Monatsblätter für Augenheilkunde* 2005; 222(12): 993-1001.
- Henneken M, Dorner T, Burmester GR, Berek C. Differential expression of chemokine receptors on peripheral blood B cells from patients with rheumatoid arthritis and systemic lupus erythematosus. *Arthritis Res Ther.* 2005;7(5):R1001-13. Epub 2005 Jun 22.
- Herlyn K, Höder J, Gross WL, Reinhold-Keller E (2005) Ein neues Schulungsprogramm – ein Statusbericht: Vaskulitis. *Z Rheumatol* 64:198-201.


- Ho Lee Y, Witte T, Momot T, Schmidt RE, Kaufman KM, Harley JB, Sestak AL. The mannose-binding lectin gene polymorphisms and systemic lupus erythematosus: Two case-control studies and a meta-analysis. *Arthritis Rheum.* 2005; 52:3966-74.
- Holle J, Hellmich B, Backes M, Gross WL, Csernok E (2005) Variations in performance characteristics of commercial enzyme immunoassay kits for the detection of antineutrophil cytoplasmic antibodies: What is the optimal cut-off? *Ann Rheum Dis*, 64: 1773-9.
- Jaeckel W H, Mau W, Zink A, Beyer W, Droste U, Engel M, Genth E. Routineberichterstattung zur medizinischen Rehabilitation bei muskuloskeletalen Krankheiten. *Z Rheumatol* 2005; 64(5): 345-350.
- Jagiello P, Aries P, Arning L, Csernok E, Hellmich B, Wagenleiter S, Gross WL, Epplen J (2005) The PTPN22 620W allele is a risk factor for Wegener's granulomatosis. *Arthritis & Rheum* 52:4039-4043.
- Jagiello P, Gross WL, Epplen J (2005) Complex genetics of Wegener's granulomatosis. *Autoimmun Rev* 4:42-47.
- Jagiello P, Klein W, Schultz H, Csernok E, Gross WL, Epplen J (2005) Association study of Wegener granulomatosis and the functionally relevant A645G polymorphism in the bactericidal/permeability increasing protein (BPI) gene. *Int J Immunogenet* 32:3-6.
- Jagiello P, Wieczorek S, Yu P, Csernok E, Gross WL, Epplen J (2005) Association study with Wegener granulomatosis of the human phospholipase Cgamma2 gene. *J Negat Results Biomed* 9:1.
- Jendro, M.C., E. Raum, S. Schnarr, L. Köhler, H. Zeidler, J. Kuipers, M. Martin. Cytokine profile in serum and synovial fluid of arthritis patients with Chlamydia trachomatis infection. *Rheumatol. Int.* 25: 37-41, 2005.
- Kamradt, T., and D. Schubert. 2005. The role and clinical implications of G6PI in experimental models of rheumatoid arthritis. *Arthritis Res* 7:20-28.
- Koch S, Goedde R, Nigmatova V, Epplen JT, Müller N, de Seze J, Vermersch P, Momot T, Schmidt RE, Witte T. Association of multiple sclerosis with ILT6 deficiency. *Genes Immun.* 2005; 6:445-7.
- Kohler S, Thiel A, Rudwaleit M, Sieper J, Braun J. CD27+ memory and CD27- effector CD8+ T cells are responsible for a decreased production of proinflammatory cytokines in HLA B27-positive subjects. *Clin Exp Rheumatol.* 2005 Nov-Dec;23(6):840-6.
- Kohler S, Wagner U, Pierer M, Kimmig S, Oppmann B, Möwes B, Jülke K, Romagnani C, Thiel A. In vivo homeostatic proliferation of naive Th-cells restrains the TCR repertoire in healthy human adults. *Eur J Immunol.*
- Mau W, Listing J, Huscher D, Zeidler H, Zink A. Employment across chronic inflammatory rheumatic diseases and comparison with the general population. *J Rheumatol.* 2005 Apr;32(4):721-8.
- Mau W, Listing J., Huscher D., Zeidler H., Zink A. Employment across chronic inflammatory rheumatic diseases and comparison with the general population. *J Rheumatol* 2005; 32(4): 721-728.
- Merkedal S, Ruof J, Huelsemann JL, Mittendorf T, Handelmann S, Mau W, Zeidler H. Indirect cost assessment in patients with rheumatoid arthritis (RA): comparison of data from the health economic patient questionnaire HEQ-RA and insurance claims data. *Arthritis Rheum.* 2005 Apr 15;53(2):234-40. Erratum in: *Arthritis Rheum.* 2005 Aug 15;53(4):624
- Metzler C, Arlt AC, Gross WL, Brandt J (2005) Peripheral neuropathy in patients with systemic rheumatic diseases treated with leflunomide. *Ann Rheum Dis* 64:1798-1800
- Minden K, Niewerth M, Zink A, Ganser G. Transition-Clinic – Der nicht immer einfache Übergang in die Rheumatologie für Erwachsene. *Z Rheumatol* 2005; 64(5): 327-333.
- Minden K, Niewerth M. Aus 'Kids' werden Teens - Probleme im Management. *Aktuel Rheumatol* 2005; 30: 157-161.
- Niesner U, Hardung F, Scheffold A, Radbruch A. T-cell receptor transgenic models of inflammatory disorders: relevance for atopic dermatitis? *Ernst Schering Res Found Workshop.* 2005;(50):175-91.
- Richter J, Nixdorf M, Becker A, Koch T, Monser R, Schneider M: Mobile Computing instead of paperbased documentation in German Rheumatology using DocuMed.rh. *TMF Workshop Mobile Computing in der vernetzten medizinischen Forschung, Berlin* <http://www.tmf-ev.de> (TMF WS)
- Richter J, Schalis H, Becker A, Koch T, Schneider M: Rheumanet.org - Medizinische online Community für entzündlich-rheumatische Systemerkrankungen: Analyse der Email-Anfragen an das Rheumatologische Expertenteam. *Z Rheumatol* 64, Suppl. 1 (2005): I/95-96. (DGRh Kongress 2005)
- Rihl M., Kruithof E., Barthel C., De Keyser F., Veys E.M., Zeidler H., Yu D.T.Y., Kuipers J.G., Baeten D. Involvement of neurotrophins and their receptors in Spondyloarthritis synovitis: relation to inflammation and response to therapy. *Ann Rheum Dis* 2005;64:1542-9.
- Rihl M., Kellner H., Kellner W., Baeten D., Barthel C., Yu D.T.Y., Zeidler H. Genexpressionsanalysen aus dem Iliosakralgelenk von Patienten mit Sakroiliitis. *Aktuelle Rheumatologie* 2005

Rudwaleit M, Baraliakos X, Listing J, Brandt J, Sieper J, Braun J. Magnetic resonance imaging of the spine and the sacroiliac joints in ankylosing spondylitis and undifferentiated spondyloarthritis during treatment with etanercept. *Ann Rheum Dis*. 2005 Sep;64(9):1305-1050:

Rudwaleit M, Baraliakos X, Listing J, Märkerl-Hermann E, Zeidler H, Sieper J, Braun J. The course of radiographic spinal lesions in patients with early ankylosing spondylitis. *Z Rheumatol*. 2005;64(suppl 1):I/17

 Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis: do we need new criteria? *Arthritis Rheum*. 2005 Apr; 52(4):1000-8.

Rudwaleit M, Niewerth M, Listing J, Märkerl-Hermann E, Zeidler H, Zink A, Braun J, Sieper J. Disease activity over one year in early ankylosing spondylitis in an observational cohort (GESPIC). *Z Rheumatol* 2005; 64(suppl 1):I/17

 Rudwaleit M, Schwarzlose S, Listing J, Brandt J, Braun J, Sieper J. Do patients with ankylosing spondylitis (AS) without elevated CRP and without active inflammation as detected by magnetic resonance imaging (MRI) respond to TNF alpha blockers? *Z Rheumatol* 2005;64(suppl 1): I/89

Rudwaleit M, Sieper J. [Diagnosis and treatment of ankylosing spondylitis (Bechterew disease)] *Dtsch Med Wochenschr*. 2005 Aug 19;130(33):1882-6. 39:

Rudwaleit M, Sieper J. [Early diagnosis of spondyloarthritis with special attention to the axial forms] *Z Rheumatol*. 2005 Nov;64(8):524-30

Rudwaleit M, Sieper J. Infliximab for the treatment of ankylosing spondylitis. *Expert Opin Biol Ther*. 2005 Aug;5(8):1095-109

Rudwaleit M. Diagnostic And Classification Criteria For Ankylosing Spondylitis And Axial Spondyloarthritis. *Ann Rheum Dis* 2005;64(Suppl III):42

Rudwaleit M. Therapy of early spondyloarthritis. *Ann Rheum Dis* 2005; 64(Suppl III):48

Rudwaleit1 M., M. Niewerth 2 , J. Listing 2 , E. Märker-Hermann 3, H. Zeidler 4 , A. Zink 2 , J. Braun 5 , J. Sieper. Disease activity over one year in early ankylosing spondylitis in a prospective observational cohort (GESPIC) *Ann Rheum Dis* 2005; 64(Suppl III):65.

Schädlich PK, Zeidler H, Zink A, Gromnica-Ihle E, Schneider M, Straub C, Brecht JG, Huppertz E. Modelling cost effectiveness and cost utility of sequential DMARD therapy including leflunomide for rheumatoid arthritis in Germany. II. The contribution of leflunomide to efficiency. *Pharmacoeconomics* 2005; 23(4): 395-420.

Schädlich PK, Zeidler H, Zink A, Gromnica-Ihle E, Schneider M, Straub C, Brecht JG, Huppertz E. Modelling cost effectiveness and cost utility of sequential DMARD therapy including leflunomide in rheumatoid arthritis in Germany. I. Selected DMARDs and patient-related costs. *Pharmacoeconomics* 2005; 23(4): 377-393.

Scheel AK, Hermann KG, Kahler E, Pasewaldt D, Fritz J, Hamm B, Brunner E, Müller GA, Burmester GR, Backhaus M: A novel ultrasonographic synovitis score suitable for analyzing rheumatoid arthritis finger joint inflammation. *Arthritis Rheum* 2005; 52(3):733-43.

Scheffold A., Hühn, J., Höfer T. (2005) Regulation of CD4+CD25+ regulatory T cell activity: it takes (IL-)two to tango. *Eur J Immunol* 35(5):1336-41.

Schnarr S, Schmidt C, Lakomek HJ, Rudwaleit M, Sieper J, Zeidler H. Bedeutung eines Antikörpers gegen ein 28KD Drosophila Antigen für die Diagnose und Verlauf von Spondyloarthritis. *Z Rheumatol* 2005;64 (suppl 1): I/87

Schneider M, Lelgemann M, Abholz HH, Caratti R, Flügge C, Jäniche H, Kunz R, Krüger K, Rehart S, Specker C. Interdisziplinäre Leitlinie Management der frühen rheumatoiden Arthritis. Steinkopff Verlag Darmstadt, ISBN 3-7985-1497-6.








Sieper J, Baraliakos X, Listing J, Brandt J, Haibel H, Rudwaleit M, Braun J. Persistent reduction of spinal inflammation as assessed by magnetic resonance imaging in patients with ankylosing spondylitis after 2 yrs of treatment with the anti-tumour necrosis factor agent infliximab. *Rheumatology (Oxford)*. 2005 Dec; 44(12):1525-30

Sieper J, Rudwaleit M. [Early diagnosis of rheumatic diseases-relevance and challenges] *Z Rheumatol*. 2005 Nov; 64(8):513-535


Sieper J, Rudwaleit M. Die ankylosierende Spondylitis (Morbus Bechterew) – diagnostisches Vorgehen und therapeutische Optionen bei einer häufig übersehenen Ursache von Rückenschmerz. *Z Allg Med* 2005; 81:65-70







Sieper J, Rudwaleit M. Early referral recommendations for ankylosing spondylitis (including pre-radiographic and radiographic forms) in primary care. *Ann Rheum Dis*. 2005 May;64(5):659-63

Sieper J, Rudwaleit M. How early should ankylosing spondylitis be treated with tumour necrosis factor blockers? *Ann Rheum Dis*. 2005 Nov;64 Suppl 4:iv61-4. Sieper J, Rudwaleit M. How early should ankylosing spondylitis be treated with tumour necrosis factor blockers? *Ann Rheum Dis*. 2005 Nov;64 Suppl 4:iv61-4.

-  Straub RH, Baerwald C, Wahle M, Jänig W. Autonomic dysfunction in rheumatic diseases. *Rheum Dis Clin North Am* 2005; 31:61-75.
- Straub RH, Wahle M, Baerwald CGO. Pathophysiologie der rheumatoiden Arthritis unter Betrachtung von neuroendokrinoimmunologischen Interaktionen. In: Straub RH (Hrsg.) *Lehrbuch der klinischen Pathophysiologie komplexer chronischer Erkrankungen*. Göttingen, Vandenhoeck & Ruprecht
- Thiel A, Alexander T, Schmidt CA, Hiepe F, Arnold R, Radbruch A, Verda L, Burt RK. Immune Reconstitution after Hematopoietic Stem Cell Transplantation in Stem Cell Transplantation for Autoimmune Disease. Editor: Richard Burt 2005
-  Thiele K, Buttgerit F, Huscher D, Zink A für die Arbeitsgemeinschaft Regionaler Kooperativer Rheumazentren. Verordnung von Glucocorticoiden bei rheumatologisch betreuten Patienten mit rheumatoider Arthritis in Deutschland. *Z Rheumatol* 2005; 64(3): 149-154.
-  Thiele K, Buttgerit F, Huscher D, Zink A. Current use of glucocorticoids in patients with rheumatoid arthritis in Germany. *Arthr Care Res* 2005; 53(5): 740-747.
-  von Mikecz A. Xenobiotic-induced autoimmunity and protein aggregation diseases share a common subnuclear pathology. *Autoimmun Rev*. 2005 Apr; 4(4):214-8. Epub 2004 Dec 15. Review.
-  Wahle M, Neumann RP, Moritz F, Krause A, Buttgerit F, Baerwald CG. Beta2-adrenergic receptors mediate the differential effects of catecholamines on cytokine production of PBMC. *J Interferon Cytokine Res*. 2005 Jul;25(7):384-94.
-  Werwitzke S, Trick D, Kamino K, Matthias T, Kniesch K, Schlegelberger B, Schmidt RE, Witte T. Inhibition of lupus disease by anti-double-stranded DNA antibodies of the IgM isotype in the (NZB x NZW)F(1) mouse. *Arthritis Rheum*. 2005; 52:3629-38.
- Witte T. Aktuelle und rationelle Diagnostik des Sjögren-Syndroms und seiner Manifestationen. *Aktuelle Rheumatologie* 2005; 30:38-40.
- Witte T. Antifodrin Antibodies in Sjögren's Syndrome: A Review. *Ann N Y Acad Sci*. 2005; 1051:235-9.
- Witte T. Antikörper gegen alpha-Fodrin als diagnostischer Marker des Sjögren-Syndroms. *Augenspiegel* 09/2005; 46-47.
- Witte T. Antikörper gegen alpha-Fodrin als diagnostischer Test des Sjögren-Syndroms. *Ophthalmologische Nachrichten*. 2005.
- Zandman-Goddard G, Blank M, Langevitz P, Slutsky L, Pras M, Levy Y, Shovman O, Witte T, Doria A, Rovinsky J, Shoenfeld Y. Anti-serum amyloid component P antibodies in patients with systemic lupus erythematosus correlate with disease activity. *Ann Rheum Dis*. 2005; 64:1698-702
-  Zink A, Huscher D, Thiele K, Listing J, Schneider M für die Arbeitsgemeinschaft regionaler kooperativer Rheumazentren. Evaluation der Prozess- und Outcomequalität der rheumatologischen Versorgung mit Hilfe standardisierter Patientendokumentation. *Arthritis + Rheuma* 2005; 25(1): 11-18.
- Zink A, Listing JD, Kary S, Ramlau P, Stoyanova-Scholz M, von Hinueber U, Babinsky K, Gromnica-Ihle E, Wassenberg S, Antoni C, Herzer P, Kekow J, Schneider M, Rau R. Treatment continuation in patients receiving biologicals or conventional DMARD therapy. *Ann Rheum Dis*. 2005 Feb 11.
- Zou J, Appel H, Rudwaleit M, Thiel A, Sieper J. Analysis of the CD8+ T cell response to the G1 domain of aggrecan in ankylosing spondylitis. *Ann Rheum Dis*. 2005 May; 64(5):722-9

Publications 2006

-  Akkad DA, Jagiello P, Szyld P, Goedde R, Wieczorek S, Gross WL, JT Epplen (2006) The promoter polymorphism rs3087456 in the MHC class II transactivator gene is not associated with susceptibility for selected autoimmune diseases in German patient groups. *Int J Immunogenet* 33: 59-61
- Appel H, Kuhne M, Spiekermann S, Ebhardt H, Grozdanovic Z, Kohler D, Dreimann M, Hempfing A, Rudwaleit M, Stein H, Metz-Stavenhagen P, Sieper J, Loddenkemper C. Immunohistologic analysis of zygapophyseal joints in patients with ankylosing spondylitis. *Arthritis Rheum*. 2006 Sep;54(9):2845-51.
- Appel H, Loddenkemper C, Grozdanovic Z, Ebhardt H, Dreimann M, Hempfing A, Stein H, Metz-Stavenhagen P, Rudwaleit M, Sieper J. Correlation of histopathological findings and magnetic resonance imaging in the spine of patients with ankylosing spondylitis. *Arthritis Res Ther*. 2006;8(5):R143.
- Appel H., H. Haibel, R. Scheer, M. Rudwaleit, J. Sieper. TNF-Antagonist therapy in patients with ankylosing spondylitis – in vitro observations of t-cell responsiveness to recall antigens during therapy. *Ann Rheum Dis* 2006; 65(Suppl II):205
- Appel1, Heiner, Christoph Loddenkemper1, Maren Kuhne1, Dorothee Köhler1, Harald Ebhardt1, Simone Spiekermann1, Marc Dreimann2, Peter Metz-Stavenhagen2, Martin Rudwaleit1, Joachim Sieper1 Inflammation in the Spine of Patients with Ankylosing Spondylitis (AS): Correlation of Histopathology with Findings in Magnetic Resonance Imaging (MRI). *Arthritis Rheum* 2006; 52(suppl); S691.
-  Aries P, Csernok E, Gross WL, Autoantibodies second edition Edit. Y Shoenfeld, ME Gershwin, PL Meroni 2006, Antineutrophil Cytoplasmic Autoantibodies with specificity to proteinase 3 PP 119-129.
- Aries PM, Witte T, Lamprecht P. [Report on the 34th Meeting of the German Clinical Immunology Workgroup, Frankfurt, 03.–04.11.2006. *Z Rheumatol*. 2006
- Baraliakos1, Xenofon, Joachim Listing2, Jan Brandt1, Martin Rudwaleit3, Henning Zeidler4, Joachim Sieper3, Jürgen Braun1. Less Radiographic Progression in Patients with Active Ankylosing Spondylitis after 2 Years of Anti-tnf Therapy. *Arthritis Rheum* 2006; 52(suppl); S631.
- Brandt H.C., H. Haibel, I. Spiller, I. Song, H. Appel, M. Rudwaleit, J. Sieper. Performance of referral recommendations for axial spondyloarthritis in patients with chronic back pain in primary care. *Ann Rheum Dis* 2006; 65(Suppl II):208
- Brandt HC., Haibel H., Spiller I., Song IH., Appel H., Rudwaleit M., Sieper J. Screening-Parameter zur Detektion von entzündlichen Wirbelsäulenerkrankungen (Spondyloarthritis) bei Patienten mit chronischen Rückenschmerzen – effektiver Einsatz in der täglichen klinischen Praxis. *Z Rheumatol* 2006; 65(suppl 1):S22
- Brandt HC., Haibel H., Spiller I., Song IH., Appel H., Rudwaleit M., Sieper J. Vergleich von Patienten mit etablierter (radiografischer) und früher (prä-radiografischer) ankylosierender Spondylitis (AS) in einer Kohorte aus der Berliner Klinik für entzündlichen Rückenschmerz. *Z Rheumatol* 2006; 65(suppl 1):S23
- Brandt, Henning C., Hildrun Haibel, Inge Spiller, In-Ho Song, Heiner Appel, Martin Rudwaleit, Joachim Sieper. Comparison of Patients with Established (Radiographic) and Early (Pre-Radiographic) Ankylosing Spondylitis (AS) in a Cohort from the Berlin Inflammatory Back Pain Clinic. *Arthritis Rheum* 2006; 54(suppl); S713.
- Brandt, Henning C., Hildrun Haibel, Silke Zinke, Inge Spiller, Martin Rudwaleit, Joachim Sieper. Early Referral Recommendations for Axial Spondyloarthritis in Patients with Chronic Back Pain – Performance in Daily Clinical Practice. *Arthritis Rheum* 2006; 52(suppl); S494.
- Braun J, Zochling J, Marker-Hermann E, Stucki G, Böhm H, Rudwaleit M, Zeidler H, Sieper J. [Recommendations for the management of ankylosing spondylitis after ASAS/EULAR: evaluation in the German language area.] *Z Rheumatol*. 2006 Dec;65(8):728-742.
- Braun J., X. Baraliakos, J. Listing, J. Davis, D. Van der Heijde, H. Haibel, M. Rudwaleit, J. Sieper. The incidence of flares or new onset of inflammatory bowel diseases in patients with ankylosing spondylitis exposed to anti-TNFA therapy. *Ann Rheum Dis* 2006; 65(Suppl II):86
- Burkhardt H, Hüffmeier U, Spriewald B, Böhm B, Rau R, Kallert S, Engström A, Holmdahl R, Reis A. Association between protein tyrosine phosphatase 22 variant R620W in conjunction with the HLA-DRB1 shared epitope and humoral autoimmunity to an immunodominant epitope of cartilage-specific type II collagen in early rheumatoid arthritis. *Arthritis Rheum.*; 54: 82-9 (2006)
-  Csernok E, Ai M, Gross WL, Wicklein D, Petersen A, Lindner B, Lamprecht P, Holle J, Hellmich B (2006) Wegener's autoantigen induces maturation of the dendritic cells and licenses them for TH1 priming via the protease-activated receptor-2 pathway. *Blood* 107:4440-4448.
-  Csernok E, Lamprecht P, Gross WL (2006) Diagnostic significance of ANCA in vasculitis. *Nature Clin Pract Rheumatol* 2:174-175.

- Haibel H, Rudwaleit M, Brandt HC, Grozdanovic Z, Listing J, Kupper H, Braun J, Sieper J. Adalimumab reduces spinal symptoms in active ankylosing spondylitis: clinical and magnetic resonance imaging results of a fifty-two-week open-label trial. *Arthritis Rheum.* 2006 Feb; 54(2):678-81
-  Haibel H.1, Brandt HC.1, Song IH.1, Brandt A.2, Listing J.3, Rudwaleit M.1, Sieper J.1, Results of an open label pilot study with 20 mg Methotrexate parenterally for the Treatment of Active Ankylosing Spondylitis. *Ann Rheum Dis* 2006;65(Suppl II):219
- Haibel H.1, Brandt HC.1, Song IH.1, Brandt A.2, Listing J.3, Rudwaleit M.1, Sieper J.1, Results of an open label pilot study with 20 mg Methotrexate parenterally for the Treatment of Active Ankylosing Spondylitis. *Z Rheumatol* 2006;65(suppl 1):S6
-  Haibel1, Hildrun, Henning C. Brandt1, In-Ho Song1, Andreas Brandt2, Joachim Listing3, Martin Rudwaleit1, Joachim Sieper1. Methotrexate 20 mg S.c. in Ankylosing Spondylitis – No Efficacy Over 4 Months Treatment in an Open Label Pilot Study. *Arthritis Rheum* 2006;54 (suppl); S724.
-  Huscher D, Merkesdal S, Thiele K, Zeidler H, Schneider, M., Zink A for the German Collaborative Arthritis Centres. Cost-of-illness in rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and systemic lupus erythematosus in Germany. *Ann Rheum Dis* 2006; 65(9): 1175-1183.
-  Huscher D, Thiele K, Weber C, Zink A (2006). Geschlechtsspezifische Unterschiede in Krankheitspräsentation und Behandlung bei Patienten mit rheumatoider Arthritis – Ergebnisse der Kerndokumentation der Rheumazentren des Jahres 2003. In: Regitz-Zagrosek V, Fuchs J, Hrsg.: *Geschlechterforschung in der Medizin.* Frankfurt/Main (Peter Lang), S. 133-43.
- Lorenz HM, Minden K, Schuch F, Hofmann S, Grifka J, Fiehn C. Kongressbericht zum 4. gemeinsamen Workshop des Kompetenznetzes Rheuma und der Arbeitsgemeinschaft kooperativer Rheumazentren. *Z Rheumatol* 2006; 3: 225-230.
-  Minden K, Niewerth M, Ganser G, Foeldvari I, Thon A, Zink A, Kinderreumatologen der Gesellschaft für Kinder- und Jugendrheumatologie. Die Kerndokumentation rheumakrankter Kinder und Jugendlicher – Bilanz nach acht Jahren. *Kinder- und Jugendmagazin* 2006; 5: 312-317.
- Minden K. What are the costs of childhood-onset rheumatic disease? *Best Pract Res Clin Rheumatol* 2006; 20(2): 223-240.
-  Momot T, Ahmadi-Simab K, Gause A, Gross WL, Gromnica-Ihle E, Peter HH, Manger K, Zeidler H, Schmidt RE, Witte T. Lack of association of mannose binding lectin variant alleles with systemic lupus erythematosus. *Ann Rheum Dis.* 2006; 65:278-9.
- Momot T, Schmidt RE, Witte T. Regulation of killer immunoglobulin-like receptors in systemic lupus erythematosus. *J Rheumatol.* 2006; 33:1029.
- Prots I, Skapenko A, Wendler J, Mattyasovszky S, Yoné CL, Spriewald B, Burkhardt H, Rau R, Kalden JR, Lipsky PE, Schulze-Koops H. The IL4R single nucleotide polymorphism 150V is associated with rapidly erosive rheumatoid arthritis. *Arthritis Rheum.*; 54: in press (2006)
- Reng CM, Debold P, Specker C u. a. *Generische Lösungen zum Datenschutz für die Forschungsnetze in der Medizin.* MWV Medizinisch Wissenschaftliche Verlagsgesellschaft. 2006, ISBN 3-939069-04-3.
- Richter J, Nixdorf M, Becker A, Koch T, Monser R, Schneider M. Mobile Computing instead of paperbased documentation in German Rheumatology using DocuMed.rh. *Proceedings International Conference of Mobile Business 2006*
- Richter J, Nixdorf M, Becker A, Koch T, Monser R, Schneider M. Mobile Computing instead of paperbased documentation in German Rheumatology using DocuMed.rh. *World Congress of Internet in Medicine, Toronto 2006.*
- Richter J, Nixdorf M, Becker A, Koch T, Monser R, Schneider M. Mobile Computing instead of paperbased documentation in German Rheumatology using DocuMed.rh. *Ann Rheum Dis* 2006, 65 (Suppl II): 600. (ACR 2006)
- Richter J, Wessel E, Klimt R, Willers R, Schneider M. Rheuma-Check – Entwicklung und Evaluation eines deutschen Rheuma-Screening Instruments. *Med Klinik* 2006, 101 (Abstractband):86. (Internistenkongress Wiesbaden)
- Richter J., Nixdorf M., Becker A., Koch T., Monser R., Schneider M.. Mobile Computing in der Rheumatologie – Einsatz eines Tablet PC. *Z Rheumatol* 2006, 65 (Suppl 1): S22. (DGRh Kongress 2006)
- Rihs M., Klos A., Köhler L., Kuipers J.G. Infection and musculoskeletal conditions: Reactive Arthritis. *Best Pract Res Clin Rheumatol* 2006; 20:1119-37

Rihl M., Köhler L., Klos A., Zeidler H. Persistent infection of Chlamydia in reactive arthritis: unravelling the molecular mechanisms. *Annals Rheum Dis* 2006; 65:281-4

Rudwaleit M, Feldtkeller E, Sieper J. Easy assessment of axial spondyloarthritis (early ankylosing spondylitis) at the bedside. *Ann Rheum Dis*. 2006 Sep; 65(9): 1251-2.

Rudwaleit M, Metter A, Listing J, Sieper J, Braun J. Inflammatory back pain in ankylosing spondylitis: a reassessment of the clinical history for application as classification and diagnostic criteria. *Arthritis Rheum* 2006; 54(2): 569-578.

Rudwaleit M, Metter A, Listing J, Sieper J, Braun J. Inflammatory back pain in ankylosing spondylitis: a reassessment of the clinical history for application as classification and diagnostic criteria. *Arthritis Rheum*. 2006 Feb; 54(2):569-78.

Rudwaleit M, Niewerth M, Listing J, Märker-Hermann E, Zeidler H, Braun J, Sieper J. Enthesitis in early Spondyloarthritis – results from a prospective longitudinal observational study (GESPIC). *Z Rheumatol* 2006; 65(suppl 1):54

Rudwaleit M, Sieper J. Positive and negative predictive values from published studies can be misleading for decision-making in clinical practice. *Rheumatology (Oxford)*. 2006 Jun; 45(6):779-80

Rudwaleit M., M. Niewerth , J. Listing , E. Märker-Hermann, H. Zeidler, J. Braun, J. Sieper. Enthesitis in early spondyloarthritis – results from a prospective longitudinal observational study (GESPIC). *Ann Rheum Dis* 2006; 65(Suppl II):85

Rudwaleit M., M. Niewerth, J. Listing, E. Märker-Hermann, H. Zeidler, J. Braun, J. Sieper. Impact of smoking on spondyloarthritis – results from a prospective longitudinal observational study (GESPIC). *Ann Rheum Dis* 2006; 65(Suppl II):540

Rudwaleit M., Wenz J., Brandt H., Appel H., Zinke S., Karberg K., Spiller I., Sieper J. Evaluation of the diagnostic algorithm and the probability approach (likelihood ratio product) in diagnosing patients with early ankylosing spondylitis. *Z Rheumatol* 2006; 65(suppl 1):55

Rudwaleit M., Wenz J., Brandt H., Appel H., Zinke S., Karberg K., Spiller I., Sieper J. Sensitivity and specificity of magnetic resonance imaging (MRI) of the sacroiliac (SI) joints in patients with suspected early ankylosing spondylitis (AS). *Z Rheumatol* 2006;65(suppl 1):525

Rudwaleit, Martin, Julia Wenz, Janis Vahldiek, Henning Brandt, Heiner Appel, Hildrun Haibel, In-Ho Song, Silke Zinke, Kirsten Karberg, Inge Spiller, Joachim Sieper. Evaluation of the Diagnostic Algorithm and the Probability Approach (Likelihood Ratio Product) in Diagnosing Patients With Early Ankylosing Spondylitis. *Arthritis Rheum* 2006; 54(suppl); S468.

Rudwaleit, Martin, Janis Vahldiek, Julia Wenz, Henning Brandt, Heiner Appel, Hildrun Haibel, In-Ho Song, Silke Zinke, Kirsten Karberg, Inge Spiller, Joachim Sieper. Sensitivity and Specificity of Magnetic Resonance Imaging (MRI) of the Sacroiliac Joints in Patients With Suspected Early Ankylosing Spondylitis. *Arthritis Rheum* 2006;54(suppl);S793.

Rudwaleit1, Martin, Robert Landewé2, Jan Brandt3, Ruben Burgos-Vargas4, Eduardo Collantes-Estevez5, Ben Dijkmans6, Maxime Dougados7, Muhammad A. Khan8, Marjatta Leirisalo-Repo9, Walter Maksymowych10, Herman Mielants11, Ignazio Olivieri12, Sjef van der Linden2, Désirée van der Heijde2, Joachim Sieper1 Assessment of Agreement of Expert Opinion on Clinical Features in Axial Spondyloarthritis (SpA). *Arthritis Rheum* 2006; 52(suppl); S637.


Rudwaleit1, Martin, Robert Landewé2, Jan Brandt3, Ruben Burgos-Vargas4, Eduardo Collantes-Estevez5, Ben Dijkmans6, Maxime Dougados7, Muhammad A. Khan8, Marjatta Leirisalo-Repo9, Walter Maksymowych10, Herman Mielants11, Ignazio Olivieri12, Sjef van der Linden2, Désirée van der Heijde2, Joachim Sieper1 Parameters Contributing to Inflammatory Back Pain (IBP) According to Experts. *Arthritis Rheum* 2006; 52(suppl); S494.

Schneider M, Lelgemann M, Abholz HH, Caratti R, Flügge C, Jäniche H, Kunz R, Krüger K, Rehart S, Specker C. Interdisziplinäre Leitlinie Management der frühen rheumatoiden Arthritis. (2. überarbeitete Auflage). Steinkopff Verlag Darmstadt, ISBN 978-3-7985-1710-3

Sieper J, Rudwaleit M, Khan MA, Braun J. Concepts and epidemiology of spondyloarthritis. *Best Pract Res Clin Rheumatol*. 2006 Jun; 20(3):401-17

Song I., H. Haibel, J. Brandt, J. Braun, J. Sieper, M. Rudwaleit. New onset of crohn's disease in three patients with ankylosing spondylitis during treatment with etanercept. *Ann Rheum Dis* 2006;65(Suppl II):543

Song I., M. Rudwaleit, J. Sieper. Comparison of the basdai and the modified basdai (mini-basdai) in assessing disease activity in patients with ankylosing spondylitis without peripheral manifestations. *Ann Rheum Dis* 2006; 65(Suppl II):543

- Song IH., Haibel H., Hilgert E., Sieper J., Rudwaleit M. Validation of the spinal pain score (spips) as an instrument performed by the rheumatologist to assess disease activity in ankylosing spondylitis. *Z Rheumatol* 2006;65(suppl 1):S25
- Song IH., Haibel H., Hilgert E., Sieper J., Rudwaleit M. Validation of the spinal pain score (spips) as an instrument performed by the rheumatologist to assess disease activity in ankylosing spondylitis. *Z Rheumatol* 2006; 65(suppl 1):S6
- Song IHS., Rudwaleit MR., Sieper JS. Vergleich des basdai und des modifizierten basdai (mini-basdai) zur Erfassung der Krankheitsaktivität bei Patienten mit ankylosierender Spondylitis ohne periphere Manifestationen. *Z Rheumatol* 2006; 65(suppl 1):S24
- Song, In-Ho, Hiltrun Haibel, Elke Hilgert, Joachim Sieper, Martin Rudwaleit. Validation of the Spinal Pain Score (spips) as an Instrument Performed by the Rheumatologist to Assess Disease Activity in Ankylosing Spondylitis. *Arthritis Rheum* 2006; 54(suppl); S474.
- Song, In-Ho, Martin Rudwaleit, Joachim Sieper. Comparison of the Basdai and the Modified Basdai (mini-BASDAI) in Assessing Disease Activity in Patients With Ankylosing Spondylitis Without Peripheral Manifestations. *Arthritis Rheum* 2006; 54(suppl); S474.
-  Szyld P, P Jagiello, E Csernok, WL Gross, JT Epplen (2006) On the Wegener granulomatosis associated region on chromosome 6p21.3. *BMC Med Genet* 7: 21
-  Ullrich S, Schumacher U, Maixing A, Gay S, Kirkiles Smith N, Pober J, Gross WL, Csernok E (2006) Das chimäre Pfp/Rag2 -/- Mausmodell als neues System zum Verständnis vaskulär entzündlicher Prozesse. *Z Rheumatol* 65:S53.
-  Westhoff G, Weber C, Zink A. Komorbidität bei früher rheumatoider Arthritis. *Z Rheumatol* 2006; 65(6): 487-496.
- Witte T, Bierwirth J, Schmidt RE, Matthias T. Antibodies against alpha-fodrin are associated with dry eyes and mouth in the general population. *J Rheumatol.* 2006 33:1713.
- Wittkop, U., B. Krause-Opatz, T. Gust, T. Kirsch, L. Köhler, M. Zenke, H. Zeidler, A. Wagner. Fate of Chlamydia pneumoniae in Human monocyte-derived dendritic cells: Productive infection over more than three weeks. *Microbial Pathogenesis* 40: 101-109, 2006.
-  Zink A, Huscher D, Schneider M. Die Kerndokumentation der Rheumazentren - Bilanz nach 12 Jahren. *Z Rheumatol* 2006; 65(2): 144-151.
-  Zink A, Thiele K, Huscher D, Listing J, Sieper J, Krause A, Gromnica-Ihle E, von Hinueber U, Wassenberg S, Genth E, Schneider M. Healthcare and burden of disease in psoriatic arthritis. A comparison with rheumatoid arthritis and ankylosing spondylitis. *J Rheumatol* 2006; 33(1): 86-90.

Publications 2007

Althoff CE, Appel H, Rudwaleit M, Sieper J, Eshed I, Hamm B, Hermann KG. Whole-body MRI as a new screening tool for detecting axial and peripheral manifestations of spondyloarthritis. *Ann Rheum Dis*. 2007 Jul;66(7):983-5

Amtenbrink A.L., Backhaus M., Brandt H.C., Song I., Appel H., Spiller I., Burmester G.R., Sieper J., Rudwaleit M. The value of power doppler ultrasonography of the heel for making a diagnosis of axial spondyloarthritis. *Ann Rheum Dis* 2007; 66(Suppl II):387

Baraliakos X, Listing J, Brandt J, Haibel H, Rudwaleit M, Sieper J, Braun J. Radiographic progression in patients with ankylosing spondylitis after 4 yrs of treatment with the anti-TNF- α antibody infliximab. *Rheumatology (Oxford)*. 2007 Sep;46(9):1450-3

Baraliakos X, Listing J, Rudwaleit M, Brandt J, Alten R, Burmester G, Gromnica-Ihle E, Haibel H, Schewe S, Schneider M, Sorensen H, Zeidler H, Visvanathan S, Sieper J, Braun J. Safety and efficacy of readministration of infliximab after longterm continuous therapy and withdrawal in patients with ankylosing spondylitis. *J Rheumatol*. 2007 Mar; 34(3):510-5.

Baraliakos X, Listing J, Rudwaleit M, Haibel H, Brandt J, Sieper J, Braun J. Progression of radiographic damage in patients with ankylosing spondylitis: defining the central role of syndesmophytes. *Ann Rheum Dis*. 2007 Jul; 66(7):910-5.

Baraliakos X., J. Listing, M. Rudwaleit, H. Haibel, J. Sieper, J. Braun. Progression of radiographic damage in patients with ankylosing spondylitis - defining the central role of syndesmophytes. *Ann Rheum Dis* 2007;66(Suppl II):85


Bierwirth J, Ulbricht KU, Schmidt RE, Witte T. Association of common variable immunodeficiency with vitamin B(6) deficiency. *Eur J Clin Nutr*. 2007


Brandt H.C., I. Song, I. Spiller, H. Appel, J. Vahldiek, J. Sieper, M. Rudwaleit. Evaluation of clinical tests for sacroiliitis and spinal mobility for diagnosing axial spondyloarthritis (spa). *Ann Rheum Dis* 2007;66 (Suppl II):390

Brandt H.C., I. Song, I. Spiller, H. Appel, J. Vahldiek, M. Rudwaleit, J. Sieper. Similar clinical presentations in established (radiographic) and early (pre-radiographic) ankylosing spondylitis (AS). *Ann Rheum Dis* 2007; 66(Suppl II):63


Brandt HC, Spiller I, Song IH, Vahldiek JL, Rudwaleit M, Sieper J. Performance of referral recommendations in patients with chronic back pain and suspected axial spondyloarthritis. *Ann Rheum Dis*. 2007 Apr 24; [Epub ahead of print]


Braun J, Baraliakos X, Listing J, Davis J, van der Heijde D, Haibel H, Rudwaleit M, Sieper J. Differences in the incidence of flares or new onset of inflammatory bowel diseases in patients with ankylosing spondylitis exposed to therapy with anti-tumor necrosis factor alpha agents. *Arthritis Rheum*. 2007 May 15;57(4):639-47

 Ferreiro-Neira I, Calaza M, Alonso-Perez E, Marchini M, Scorza R, Sebastiani GD, Blanco FJ, Rego I, Pullmann R Jr, Pullmann R, Kallenberg CG, Bijl M, Skopouli FN, Mavromati M, Migliaresi S, Barizzone N, Ruzickova S, Dostal C, Schmidt RE, Witte T, Papasteriades C, Kappou-Rigatou I, Endreffy E, Kovacs A, Ordi-Ros J, Balada E, Carreira P, Gomez-Reino JJ, Gonzalez A. Opposed independent effects and epistasis in the complex association of IRF5 to SLE. *Genes Immun*. 2007.


 Ferreiros-Vidal I, D'Alfonso S, Papasteriades C, Skopouli FN, Marchini M, Scorza R, Migliaresi S, Sebastiani GD, Endreffy E, Mavromati M, Kappou-Rigatou I, Ruzickova S, Dostal C, Schmidt RE, Witte T, Gomez-Reino JJ, Gonzalez A. Bias in association studies of systemic lupus erythematosus susceptibility due to geographical variation in the frequency of a programmed cell death 1 polymorphism across Europe. *Genes Immun*. 2007; 8:138-46.


Gwinner W, Erdbruegger U, Mengel M, Hafer C, Kittner J, Witte T, Voelker B, Haller H. Scleroderma-like acute renal crisis in a patient with scleromyxedema. *Nephrol Dial Transplant*. 2007; 22:2063-7.

 Heberlein I, Dreher R, Zink A, Zeidler H, Pollähne W, Raspe H, für die ORA-Studiengruppe (2007) Prävalenz von Osteoporose und Osteopenie bei Patienten mit rheumatoider Arthritis. *Zeitschrift für Rheumatologie* 66, S1:101

 Heberlein I, Dreher R, Zink A, Zeidler H, Raspe H, für die ORA-Studiengruppe (2007) Osteoporoseprophylaxe und -therapie bei Patienten mit rheumatoider Arthritis. *Zeitschrift für Rheumatologie* 66, S1:14

Heiligenhaus A, Niewerth M, Ganser G, Heinz C, Minden K. Prevalence and complications of uveitis in juvenile idiopathic arthritis in a population-based nation-wide study in Germany: suggested modification of the current screening guidelines. *Rheumatology (Oxford)* 2007;

 Hellmich B, Csernok E, Fredenhagen G, Gross WL (2007) A novel high sensitivity ELISA for detection of antineutrophil cytoplasm antibodies against proteinase-3. *Clin Exp Rheumatol* 25 (1):S1-S5.

 Kahlmann D, Davalos-Misslitz AC, Ohl L, Stanke F, Witte T, Forster R. Genetic variants of chemokine receptor CCR7 in patients with systemic lupus erythematosus, Sjogren's syndrome and systemic sclerosis. *BMC Genet*. 2007; 8:33.

 Publication with reference to BMBF funding

- ✎ Kozyrev SV, Lewen S, Reddy PM, Pons-Estel B; Argentine Collaborative Group, Witte T; German Collaborative Group, Junker P, Lastrup H, Gutierrez C, Suarez A, Francisca Gonzalez-Escribano M, Martin J; Spanish Collaborative Group, Alarcon-Riquelme ME. Structural insertion/deletion variation in IRF5 is associated with a risk haplotype and defines the precise IRF5 isoforms expressed in systemic lupus erythematosus. *Arthritis Rheum.* 2007; 56:1234-41.
- ✎ Krause-Opatz, B., Busmann, A., Tammen, H., Menzel, C., Möhring, T., Le Yondre, N., Schmidt, C., Schulz-Knappe, P., Zeidler, H., Selle, H., Köhler, L. Peptidomic Analysis of Human Peripheral Monocytes persistently infected by *Chlamydia trachomatis*. *Med. Microbiol Immunol.* 196: 103-14, 2007
- ✎ Lee-Kirsch, MA, Gong, M, Chowdhury, D, Senenko, L, Engel, K, Lee YA, de Silva, U, Bailey, SL, Witte, T, Vyse, TJ, Kere, J, Pfeiffer, C, Harvey, S, Wong, A, Koskenmies, S, Hummel, O, Rohde, K, Schmidt, RE, Dominiczak, AF, Gahr, M, Hollis, T, Perrino, FW, Lieberman, J and Huber, N (2007) Mutations in the 3' to 5' DNA exonuclease TREX1 are associated with systemic lupus erythematosus, *Nature Genetics*, in press.
- ✎ Metzler C, Miehle N, Manger K, Iking-Konert C, de Groot K, Hellmich B, Gross WL, Reinhold-Keller E (2007) Elevated relapse rate under oral methotrexate versus leflunomide for maintenance of remission in Wegener's granulomatosis. *Rheumatology (Oxford)* 2007 May 22
- ✎ Minden K, Mingels A, Niewerth M, Heiligenhaus A, Ganser G. Juvenile idiopathic Arthritis und Uveitis: Epidemiologie einschließlich der Daten aus der Kerndokumentation. *Klin Monatsbl Augenheilkd* 2007; 224(6): 469-472.
- Richter J, Becker A, Koch T, Schacher B, Nixdorf M, Monser R, Schneider M. Rheumatologische Patientinnen sind bereit für ein gutes Internet-Angebot. *Z Rheumatol* 2007, in press. (DGRh Kongress 2007)
- Richter J, Becker A, Koch T, Schacher B, Nixdorf M, Monser R, Schneider M: Changing computer and internet use in German rheumatology outpatients in 2006: Gender becomes less important. *Ann Rheum Dis* 2007, 66 (Suppl II): 272. (EULAR 2007)
- Richter J, Wessel E, Klimt R, Willers R, Schneider M. Rheuma-Check Entwicklung und Evaluation eines deutschen Rheuma-Screening Instruments. *Wien klin Wochenschrift* submitted.
- Rihl M., Zeidler H. The molecular pathogenesis of *Chlamydia* induced arthritis – where do we stand? *Curr Rheumatol Rep* 2007; 9:4-5.
- ✎ Rudwaleit M, Sieper J. A case of axial undifferentiated spondyloarthritis diagnosis and management. *Nat Clin Pract Rheumatol.* 2007 May; 3(5):298-303
- ✎ Salzer U, Birmelin J, Bacchelli C, Witte T, Buchegger-Podbielski U, Buckridge S, Rzepka R, Gaspar HB, Thrasher AJ, Schmidt RE, Melchers I, Grimbacher B. Sequence Analysis of TNFRSF13b, Encoding TACI, in Patients with Systemic Lupus Erythematosus. *J Clin Immunol.* 2007; 27:372-7.
- ✎ Schnitger K, Njau F, Wittkop U, Liese A, Kuipers JG, Thiel A, Morgan MA, Zeidler H, Wagner AD. Staining of *Chlamydia trachomatis* elementary bodies: a suitable method for identifying infected human monocytes by flow cytometry. *J Microbiol Methods.* 2007 Apr; 69(1):116-21
- ✎ Schrader S., Klos A., Hess S., Zeidler H., Kuipers J.G., Rihl M. Expression of inflammatory host genes in *Chlamydia trachomatis* infected human monocytes. *Arthritis Res Ther.* 2007 May 24;9:R54
- Sieper J, Klopsch T, Richter M, Kapelle A, Rudwaleit M, Schwank S, Regourd E, May M. Comparison of 2 different dosages of celecoxib with diclofenac for the treatment of active ankylosing spondylitis: results of a 12-week randomised double-blind controlled study. *Ann Rheum Dis.* 2007 Jul 6; [Epub ahead of print]
- Sieper J, Rudwaleit M, Braun J. Adalimumab for the treatment of ankylosing spondylitis. *Expert Opin Pharmacother.* 2007 Apr; 8(6):831-8.
- Song I., H. Haibel, E. Hilgert, J. Sieper, M. Rudwaleit. Role of the physical examination of the spine in the assessment of disease activity in ankylosing spondylitis. *Ann Rheum Dis* 2007; 66(Suppl II):63
- ✎ Werwitzke S, Trick D, Sondermann P, Kamino K, Schlegelberger B, Kniesch K, Tiede A, Jacob U, Schmidt RE, Witte T. Treatment of lupus-prone NZB/NZW F1 mice with recombinant soluble Fc{gamma} receptor II (CD32). *Ann Rheum Dis.* 2007.
- ✎ Westhoff G, Rau R, Zink A. Radiographic joint damage in early rheumatoid arthritis is highly dependent on body mass index. *Arthritis Rheum* 56: 3575-82 (in press).
- ✎ Westhoff G, Zink A. Basistherapie bei früher rheumatoider Arthritis. Verzicht auf rheumatologische Mitbetreuung und Präferenz für Alternativmedizin erhöhen das Risiko einer Unterversorgung. *Z Rheumatol* 2007; 66(2): 121-128.
- ✎ Zink A, Huscher D. Die Bedeutung entzündlich-rheumatischer Erkrankungen aus sozialmedizinischer Sicht. *internist prax* 2007; 47: 319-334.