

Speaker Presentations

WEDNESDAY, 14 JUNE 2017

Joint EULAR - APLAR session: novel animal models - where no researcher has gone before... _____

SP0001 RELEVANCE OF ANIMAL MODELS IN OSTEOARTHRITIS

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Osteoarthritis (OA) is the most frequent joint disease and a leading cause of disability in the Western world. Currently, we do not have a cure for this degenerative disorder and despite a high individual and socioeconomic demand, available therapeutic strategies have not changed substantially within the last 40 to 50 years, largely involving basic symptomatic control using analgesics and NSAIDs, physiotherapy and behavioural changes, and eventual prosthetic replacement in end-stage disease. While prosthetic joint replacement constitutes an effective surgical treatment option for patients whose joints are irreversibly damaged by OA, demographic development together with altered physical activities in our aging society increasingly demonstrate the limitations of joint replacement surgery as the only real treatment modality. There is, therefore, an urgent requirement for disease modifying drugs that aim to halt OA disease progression during the early stages and potentially to kick start cartilage regeneration. This need is contrasted, however, by a sustained "translational roadblock" in OA research with very few conceptually novel therapeutic approaches on the horizon. Amongst others, this "translational roadblock" results from a general lack in our understanding of how articular chondrocytes as the only cells in joint cartilage acquire and maintain their specific and highly specialised phenotype and how this phenotype changes during OA onset and progression. Investigation of this developmental aspect of disease pathology in OA patients and using human samples has many limitations, which is why animal models remain to constitute a key element of cartilage and OA research. This lecture summarizes the relevance of different animal models for understanding fundamental principles of cartilage homeostasis and remodelling in health and osteoarthritic cartilage degeneration. By focusing on the analysis of chondrocyte phenotypic stability, it provides examples for how the use of such models can contribute to understanding OA and to the development of new therapeutic strategies for the disease.

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SP0002 NOVEL ANIMAL MODELS IN SYSTEMIC SCLEROSIS

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Systemic sclerosis (SSc) is a severe autoimmune disease with a considerable reduction of life expectancy. Autoimmunity, vasculopathy and fibrosis are three hallmarks of SSc, while the pathogenesis of the disease is largely unknown. Animal models of SSc provide an excellent tool to explore the disease pathogenesis of the disease. Aiming to provide a concise and curate updates in the field of animal models of SSc, this lecture will concentrate on emerging novel animal models and highlight new development and their impact on understanding pathogenesis of SSc.

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SP0003 NOVEL ANIMAL MODEL IN ARTHRITIS

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We have generated two rheumatoid arthritis (RA) models, human T-cell leukemia virus type I (HTLV-I) transgenic mice and IL-1 receptor antagonist (Ra)-deficient (KO) mice, to elucidate the pathogenic mechanisms of the disease. Both models spontaneously developed arthritis that closely resembles RA in humans. We found that TNF-, but not IL-6-, deficiency suppressed development of arthritis in IL-1Ra KO mice, while IL-6 but not TNF was involved in the development of arthritis in HTLV-I transgenic mouse model. IL-17 plays an important role in both models, suggesting the central role of IL-17 in these RA models.

We found that the expression of C-type lectin receptor (CLR) genes was augmented in the affected joints of these models using DNA microarrays. Dendritic cell immunoreceptor (DCIR) is one of such CLR genes with a carbohydrate recognition domain in their extracellular carboxy terminus and an ITIM in its intracellular amino terminus. Because human syntenic locus for the CLR genes is linked to several autoimmune diseases including RA and SNPs in the *Dcir* gene

is associated with RA, we have generated *Dcir* KO mice to examine the roles of this gene in the immune system. We found that aged *Dcir* KO mice spontaneously developed autoimmune enthesitis and ankyloses accompanied by fibrocartilage proliferation and ectopic ossification. DCs were excessively expanded in *Dcir* KO mice, causing these mice autoimmunity and also highly susceptible to induced-autoimmune diseases. *Dcir* KO mouse-derived bone marrow cells differentiated into DCs more efficiently than did wild-type BMCs upon treatment with GM-CSF, due to enhanced STAT-5 phosphorylation. Furthermore, we found that IFN-g producing T cells were increased in *Dcir* KO mice and IFN-g enhanced bone and cartilage formation, resulting in the increase of bone volume and aberrant ossification in joints. DCIR is also expressed in osteoclasts and suppresses osteoclastogenesis upon activation. These findings suggest that DCIR plays important roles in both immune system and bone metabolism.

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SP0004 PEPTIDYL ARGININE DEIMINASE 4 AND RHEUMATOID ARTHRITIS: FROM HUMAN GENETICS TO MURINE MODELS

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We have previously reported that functional haplotypes of peptidyl arginine deiminase 4 (*PADI4*) are associated with rheumatoid arthritis (RA). We found that transcripts of the risk haplotype of *PADI4* are more stable than those of the non-risk haplotypes, suggesting that increased expression and function of *PADI4* (encoded by *PADI4* gene) increase the risk of RA. The association has been confirmed by several studies with different ethnics. Further, we also reported *PADI4* polymorphisms highly predispose male smokers to RA. Since *PADI4* catalyzes an arginine residue in a protein to citrulline and anti-citrullinated protein antibodies (ACPA) are highly specific in RA, it has been reasonable to speculate that increased *PADI4* is associated with increased citrullinated proteins, leading to the initiations of tolerance breakdown or inflammatory arthritis.

However, the mechanisms of *PADI4* involvement turned out to be more complex than previously thought in animal models. In order to investigate the pathological process in detail, we made *Padi4* knockout mice. Decreased severity of experimental autoimmune arthritis was observed in these mice. Further, we found *PADI4* regulates the pro-apoptotic fate of neutrophils, and promotes the expression of pro-inflammatory cytokines in macrophages. These actions could result in the pro-arthritis roles of *PADI4*. Recently, neutrophil extracellular traps (NETs) were reported as an important immune stimulator in RA and SLE, and *PADI4* is required for the generation of NETs. Especially, NET-containing immune complex (IC) stimulated plasmacytoid dendritic cells to accelerate the interferon secretion in SLE. Therefore, *PADI4* could play several different roles in the immune system and also in the pathogenesis of autoimmune diseases.

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Health professional welcome session _____

SP0005 LOOKING BACK AT 70 YEARS OF EULAR AND 30 YEARS OF HP INVOLVEMENT: A REHABILITATION PERSPECTIVE

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The medical treatment of people with rheumatic and musculoskeletal diseases (RMDs) has improved enormously over the past decades. As medical treatment is not completely successful or available for all rheumatic conditions or individual patients, and the demands society imposes on people to participate fully are increasing, there is a substantial proportion of people with RMDs who have functional disabilities.

Health professionals (HPs) play an essential role in the management of people with RMDs with disabilities by enabling to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. They provide people with the tools they need to attain independence and self-determination. As such, their contribution is in line with the World Health Organisation definition of rehabilitation [http://www.who.int/topics/rehabilitation/en/]. An important feature of rehabilitation is its multidisciplinary. Over the past decades, it has been more and more acknowledged that HPs' role in the management of people with RMDs concerns a team effort rather than the summation of single interventions by individual HPs or specific professions. This view is reflected in multiple guidelines and standards of care for the clinical management of RMDs, where the need for people with RMDs to have access to a multidisciplinary team of HPs is underlined.

The acknowledgement of the importance of the team of HPs runs in parallel with developments in the organization and activities of HPs within EULAR over the past years.

In connection with EULAR, there is a growing network of HPs from multiple professions across Europe. By working together, and collaborating with patients and rheumatologists and other physicians, EULAR HPs have achieved multiple milestones with respect to the quality of clinical care, education, and research over the past years and are equipped to encounter future challenges.

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SP0006 LOOKING BACK AT 70 YEARS OF EULAR AND 30 YEARS OF HP INVOLVEMENT: A NURSING PERSPECTIVE

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At the 1987 EULAR Congress held in Athens, a British nurse, Vicky Stephenson, arranged a meeting that was attended by about 30 health professionals. The meeting decided that a working group of Health Professionals from different professions and countries should work towards establishing a Standing Committee within EULAR. This was achieved in 1989 and since that time, the role of Health Professionals within EULAR has changed dramatically.

In this lecture, I will describe the evolution of rheumatology nursing over the past thirty years, and the part that EULAR has played in the dissemination, education and facilitation of best nursing practice and experiences within Europe. This will be illustrated by two pieces of work. In late 2009, EULAR part funded a Web-based survey to evaluate the status of extended roles undertaken by health professionals in Europe. The data from this survey relating to nursing has been extracted and analysed separately and will be presented. The following year, EULAR also funded a study to investigate the role of the nurse in the management of chronic inflammatory arthritis. The important recommendations resulting from this piece of work will also be shown.

Following the recommendations project, a number of other important nursing initiatives have been launched under the auspices of EULAR. These will be highlighted to enable delegates to understand how far rheumatology nursing has developed and how far it still has to go.

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SP0007 70 YEARS PAST AND A VIEW OF THE FUTURE: LOOKING BACK AND LOOKING FORWARD

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In 1913 the Dutch general practitioner Jan van Breemen, moved by the needs of the many disabled people in his practice, started an international cooperation to fight rheumatic and musculoskeletal diseases. His initiative led to the formation of the International League Against Rheumatism (ILAR), and subsequently to the formation of regional Leagues, such as EULAR in 1947.

EULAR has in the following 70 years developed into a unique organisation of rheumatologists, scientists, health professionals and patients, who together are aiming to reduce the burden of rheumatic diseases on the individual and society and to improve the treatment, prevention and rehabilitation of musculoskeletal diseases. To this end, EULAR fosters excellence in education and research in the field of rheumatology. It promotes translation of research advances into daily care and fights for the recognition of the needs of people with RMDs by the governing bodies in Europe (EULAR mission statement 2005).

The first European Rheumatology Congress was held in September 1947 in Copenhagen and was attended by 200 delegates from 16 countries. At the EULAR 2017 Madrid Congress over 14.000 attendees are expected, coming from more than 120 countries.

EULAR is unique in the sense that three pillars work closely together in one organization: rheumatologists, health professionals and patients. Today, I want to focus a bit on the health professionals pillar, since this pillar has its formal 30 years jubilee in 2017 as well. At the American celebration of 50 years of non-physician health professionals in Rheumatology (2015), Brady described three science-driven practice paradigm shifts that play an important role in managing patients with RMDs: 1. The widely used "Self-management programs", that were developed from information giving and 'patient education'. 2. The positive and intensive use of "Exercise and physical activity", that were developed from previous acclaimed bed rest and assisted range of motion exercises. 3. The OMERACT initiated definitions and applications of Patient-reported outcome measures, instead of only biomedical assessment of disease activity.

In addition, she recognized two "evolutions in practice": 1. Understanding Psychological Factors, from accepting "the arthritic personality" to actively addressing depression, anxiety, coping skills, sense of control and confidence. 2. The development of the important role that nurses and other health professionals can play in the treatment of patients with RMDs.

The EULAR health professionals can be very proud of the important part that Europeans have played in these worldwide developments.

My priorities as president-elect of EULAR for the coming two years are:

- Further development of the School of Rheumatology

- Large public awareness campaign: Don't delay, Connect today
- New EULAR Strategy 2018–2023

I hope and expect that the pillar of health professionals will take an active role in the cooperation that is necessary to reach our common goals.

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SP0008 THE FUTURE FOR HEALTH PROFESSIONALS IN RHEUMATOLOGY

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In recent years the prevalence of rheumatic diseases has raised leading to increased outpatient activity; at the same time, a general lack of rheumatologists has been described (1). This has created new demands from patients and the health care system towards innovative models of care, e.g. nurse-led follow-up (2), direct access strategies (3) and tele-health interventions (1). In the future this will call for extended and specialized roles for health-professionals within rheumatology, and for future development of compatibility of training of health professionals within the European countries.

Further, the current health-service development is confronting the population with increasing demands to understand and utilize health information and to navigate through this increasingly complex healthcare system. It requires that patients are capable of understanding and managing their health, and calls upon a strong focus on health-literacy (HL) skills, and the formation of so-called HL organizations (4). In the future, health professionals within rheumatology will have a key role in supporting the development of HL responsive organizations through self-management strategies and patient centered care.

The present presentation will address some of these future demands for health professionals in Rheumatology

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WIN & HOT session

SP0009 WHAT IS NEW (WIN) IN PSORIATIC ARTHRITIS

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Novel therapies and targets have transformed the management of psoriatic arthritis and related skin disease psoriasis. The successful introduction and widespread use of anti-IL17, anti-IL12/23 and anti-PDE4 strategies have joined the ranks of TNF inhibitors. Novel biological insights into specific disease mechanisms are co-emerging with this new wave of treatment options. The different available treatments allow the community to further focus on optimal patient management aiming at remission or minimal disease activity. Yet, the assessment of the patient and his/her satisfaction with current health status remains challenging. Treat to target initiatives are trying to define optimal care and cure adapted to the specific characteristics of the disease. Molecular knowledge of the disease processes remains scattered and insufficient to build a comprehensive view on the disease for the individual patient that would allow the personalized definition of effective strategies.

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