Although the literature on the outcomes of total hip and knee arthroplasty (THA and TKA) is vast, relatively little is known about physical activity levels of OA patients undergoing surgery.

This presentations summarizes the state-of-the-art literature on the physical (in) activity level of patients with an indication for TKA or THA and its determinants, and the changes of physical (in)activity levels after surgery. These results are presented taking into account the activity levels of the general population. The presentation will end with an informal quiz on physical (in)activity in THA and TKA patients.

REFERENCES:

- [1] Meessen JM, et al. *Rheumatol Int.* 2017 Feb;37(2):219-227.
- [2] Mills K, et al. *Physiotherapy.* 2019 MAR;105(1):35-45.
- [3] Hammett T, et al. *Arthritis Care Res.* 2018 Jun;70(6):892-901.
- [4] Lee J, et al. *Arthritis Care Res.* 2015;67(3):366-373.

Disclosure of Interests: None declared

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SP0051

CASE 2 DISCUSSANT: DISCUSSION OF HOW A LARGE PROPORTION OF PEOPLE DO NOT BECOME ACTIVE AFTER JOINT REPLACEMENT DESPITE ADEQUATE PAIN RELIEF, REASONS, NEGATIVE CONSEQUENCES OF REDUCED ACTIVITY AND POSSIBLE APPROACHES

Thea Vliet Vlieland. Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands

The literature on the effect of total hip and knee arthroplasty (THA and TKA) on the amount of physical activity is scanty, with various studies suggesting that physical activity levels do not increase after surgery. These results raise several questions, such as: Are patients who will undergo or underwent THA or TKA more or less physically active than the general population? And, if not, should they become more physically active, what are barriers and facilitators for physical activity levels, what would be the potential benefits? Who are the stakeholders that should be involved in the promotion of physical activity in this patient group? These, and other questions will be highlighted in an interactive discussion with the attendees of the session.

REFERENCES:

- [1] Pellegrini CA, et al. *Disabil Rehabil.* 2018;40:2004-2010.
- [2] Naylor JM, et al. *Arthritis Care Res (Hoboken).* 2019;71:207-217.
- [3] Hodges A, et al. *Clin Rehabil.* 2018;32:1271-1283.

Disclosure of Interests: None declared

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

My joints hurt and I'm overwhelmingly tired – fatigue in rheumatoid arthritis

SP0052

FATIGUE IN RHEUMATOID ARTHRITIS: WHAT IT IS AND HOW TO ASSESS IT?

José Antonio P. da Silva. Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal

Background: Fatigue is a frequent and important symptom in rheumatoid arthritis (RA), and it is associated with significantly reduced health-related quality of life, thus contributing to the impact of disease upon patients' lives.

Objectives: To collect, summarise and interpret available evidence on the nature of fatigue and the best ways to assess it in Rheumatoid Arthritis

Methods: A systematic literature research was performed in trying to (i) to synthesize the role of fatigue in the global impact of rheumatoid arthritis; (ii) describe validated instruments and their psychometric properties as measures of fatigue among patients with RA; and finally (iii) propose a clinically meaningful, valid and feasible process to measure fatigue in clinical practice.

Results: Fatigue has a major relevance in the overall burden of disease in RA. Several instruments have been validated to measure it, but no consensus has yet been reached to recommend a "gold-standard".

Conclusion: Although fatigue is recognized by the rheumatology community as an important consequence of RA and a major gap in its current management of the disease, it has not been easy to measure and grasp. The problem seems to

reside in the multidimensional causality and subjective nature of this phenomenon, which may warrant dedicated measures and interventions.

Disclosure of Interests: None declared

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SP0053

HOW TO PREVENT AND MANAGE FATIGUE IN PATIENTS WITH RA

James Galloway. King's College London, Inflammation Biology, London, United Kingdom

Background: Fatigue is, similar to pain, a subjective symptom that occurs in many different diseases, particularly in patients with RA. Indeed, RA patients consistently report fatigue as one of the most disabling features of the disease (second only to pain). Fatigue is multifactorial in origin and reflects a complex construct of psychological, biochemical and physiological processes.

Objectives: If we are to effectively support our patients with RA, we must address fatigue. This requires understanding of which of our interventions work. At the end of the talk you should be familiar with how you can help manage fatigue, know which non-pharmacological interventions have a robust evidence and be aware of the impact of our different mode of action targeted RA therapies upon fatigue. For most our patients, a multimodal approach is needed.

Methods: This talk will present a narrative review of the evidence base around fatigue interventions in RA.

Disclosure of Interests: James Galloway Consultant for: Pfizer Inc

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Molecular fingerprinting

SP0054

DECONVOLUTION OF THE IMMUNE RESPONSE

Lars Rogge. Institut Pasteur, Immunoregulation Unit, Immunology Department, 75015 Paris, France

Background: Anti-TNF therapy has revolutionized treatment of many chronic inflammatory diseases, including rheumatoid arthritis, Crohn's disease and spondyloarthritis (SpA). However, clinical efficacy of TNF-inhibitors (TNFi) is limited by a high rate of non-responsiveness (30-40%) both in SpA and other diseases, which exposes a substantial fraction of patients to important side-effects without clinical benefit. Despite TNFi having been used extensively for many years, it is still not possible to determine which patients will respond to TNFi before treatment initiation.

Objectives: In this study, we have tested the hypothesis that the functional analysis of immune responses of patients before and after anti-TNF therapy may not only improve our understanding of the molecular mechanisms of TNF-blocker activity, but also identify correlates of therapeutic responses in SpA patients.

Methods: To facilitate the potential translation of our findings into a clinical setting, we have used standardized whole-blood stimulation assays ("TruCulture" assays; Duffy et al., 2014), and have minimized sources of pre-analytical variability, implementing a highly sensitive and robust pipeline to assess immune functions in patients.

Results: We show that anti-TNF therapy induces profound changes in patients' immune responses, affecting predominantly several innate immune pathways. Of note, all these effects could be measured in stimulated, but not in resting immune cells, and were already detectable early, after a single TNFi injection. Modular transcriptional repertoire analysis revealed that TNFi affect immune responses via multiple mechanisms, such as directing monocyte/macrophage polarization and the inhibition of a TNF- and IL-1-dependent feed-forward loop of NF-κB activation.

On the other hand, the action of anti-TNF treatment was surprisingly selective, in that it did not affect the IL-6/Th17 or Th1 arm of the patients' immune response. These findings have important implications for therapy, given the recent approval of anti-IL-17 antibodies as an alternative agent for the treatment of several chronic inflammatory diseases.

To investigate the concept that the immune status of a patient will define their response to TNFi treatment, we have used machine-learning algorithms to identify, in whole-blood stimulation assays, immunological transcripts that correlate with clinical efficacy of TNFi. We found that high expression, before treatment initiation, of molecules associated with leukocyte invasion/migration and inflammatory processes predisposes to favorable outcome of anti-TNF therapy, while high-level expression of cytotoxic molecules was associated with poor therapeutic responses to TNF-blockers.

Conclusion: These findings suggest that SpA patients whose immune response is characterized by strong, NF-κB-mediated inflammation are more likely to benefit

from TNFi treatment than patients with an active T/NK-cell component. This proof-of-concept study establishes a new framework to explore patient stratification in chronic inflammatory diseases according to the patients' immune phenotype.

REFERENCE:

- [1] Duffy, D., et al. Functional Analysis via Standardized Whole-Blood Stimulation Systems Defines the Boundaries of a Healthy Immune Response to Complex Stimuli. *Immunity* 40, 436-450 (2014).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.8574

SP0055 CLINICAL MULTI-OMICS

Timothy R. Radstake. *University Medical Center Utrecht, Netherlands*

It is becoming clear that the field of medicine needs to change to stay affordable. One way of doing that is by optimizing the patients journey with true personalized medicine approaches. In other words, how to give every patient the right drug, at the right moment for the optimal duration. Recent advances in molecular techniques have truly revolutionized research into molecular fingerprinting – classification of clinical phenomena on the basis of a molecular basis rather than a diagnosis based on organ, symptoms or clinical criteria. This makes personalized medicine reachable within the coming years.

In my presentation I will dive in to the various molecular technologies (multi-omics) to achieve molecular fingerprinting of patients. Next, I will explain the computational techniques necessary to process the big data originating from the molecular processes enabling researchers to visualize big data from clinicians and patients. Finally, I will provide several examples of how these exercises might improve care for patients covering the space of rheumatic and musculoskeletal diseases (RMDs).

At the end of my presentation I will show how big data can be used for drug discovery, immune monitoring in clinical trials and/or daily clinical practice as well as drug repurposing. Together, I will provide a glimpse of the future on personalized healthcare within the field of RMDs.

Disclosure of Interests: None declared

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SP0056 MAPPING GENES TO IMMUNE CELLS

Kazuhiko Yamamoto. *RIKEN Center for Integrative Medical Sciences, Laboratory for Autoimmune Diseases, Yokohama, Japan*

Background: Many disease susceptibility variants have been recently identified by genome wide association study (GWAS). Germline genetic variations exist before the disease onset and provide us with evidence into the causal relationship of the observed phenomenon and their pathogenesis. In this regards, the majority of GWAS risk variants have been found to function as an expression-quantitative trait locus (e-QTL).

Objectives: We need functional studies aiming at determining the causal genetic variants uncovered by GWAS and finding biological mechanisms underlying the observed statistical associations.

Methods: We established a system to evaluate various subtypes of leukocytes from peripheral blood mononuclear cells (PBMC) from healthy individuals. PBMC are separated with a fluorescence activated cell sorter and are analyzed in a steady state or activated conditions to capture the dynamic responses of gene regulation. Genotyping, RNA-seq, assay for transposase-accessible chromatin using sequencing (ATAC-seq) are performed on each subset. To further investigate the genetic determinants of promotor and enhancer activities, we also perform Cap Analysis of Gene Expression (CAGE) on the corresponding samples. CAGE is a technology developed in our research center RIKEN in Japan. It relies on random priming and cap-trapping of cDNAs to capture the 5' ends of both polyadenylated and non-polyadenylated RNA transcripts. It thus enables genome-wide identification of transcription start sites (TSSs), which could be used as a portal to annotate and measure the activity of promoters and enhancers (Carninci P. et al Science 2005, Forrest ARR. et al Nature 2014 and other publications of the FANTOM project). Using CAGE, we can map the promoters, enhancers and lncRNAs active in each leukocyte subtypes and correlate their activities with genetic variants.

Results: I will present our ongoing data.

REFERENCES:

- [1] Okada Y, et al. Genetics of rheumatoid arthritis contributes to biology and drug discovery. *Nature* 2014;506:376-381.
[2] Ishigaki K, et al. Polygenic burdens on cell-specific pathways underlie the risk of rheumatoid arthritis. *Nat Genet* 2017;49:1120-1125.

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Adults are just grown up children! Discuss

SP0057 EVERYTHING STARTS IN CHILDHOOD!

Berent J. Prakken. *University Medical Center Utrecht, Biomedical education, Utrecht, Netherlands*

Background: While part of our future may be determined by our genes, the interaction of our immune system with the environment is crucial for the balance between health and disease. Most of these crucial interaction take place in the early years of life during which the developing immune system settles between self and non-self; danger and non danger or whatever paradigm you may want to apply. This early flexibility and early interactions between developing immunity and the environment hold the key for a health future; and ultimately will be the most effective way for true (very!) early prevention of chronic inflammatory disorders.

Disclosure of Interests: None declared

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SP0058 GROWING UP CHANGES EVERYTHING!

Iain McInnes. *University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom*

Background: There is increasing interest in understanding the impact of age upon the emergence and clinical impact of immune mediated inflammatory diseases. In this lecture I will consider the similarities and distinctions between the presentation of inflammatory arthritis in children and adults.

Disclosure of Interests: Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma

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THURSDAY, 13 JUNE 2019

13:30:00 – 15:00:00

Exercise – more than a wonderdrug

SP0059 HELPING PEOPLE MAINTAIN PHYSICAL ACTIVITY

Keegan Knittle. *University of Helsinki, Faculty of Social Sciences, Helsinki, Finland*

Background: Regular physical activity (PA) has clear benefits for individuals with rheumatic diseases, but PA levels among these individuals consistently fall below recommended levels. While interventions to increase PA are often successful in the short term, these effects are not generally maintained over time. Therefore, to be able to optimally support PA maintenance, rheumatology health professionals should be familiar with the relevant theory and evidence base for behavioral maintenance.

Objectives: This talk will outline several psychological theories of behavioral maintenance, and present evidence on the interventions and behavior change techniques most strongly associated with physical activity maintenance.

Methods: A review of the most recent and relevant health psychology and behavioral science literature surrounding issues of physical activity maintenance, particularly among individuals with rheumatic conditions.

Results: Theories of behavioral maintenance focus on social and environmental influences, motives, resources, self-regulation, and habits. Several studies will be presented to highlight the influence of these theoretical domains in PA maintenance among individuals with rheumatic disease. Physical activity interventions which specifically target these theoretical domains have the greatest likelihood to produce PA maintenance, and several case studies from successful interventions will be presented.

Conclusions: While helping patients to maintain PA is always a challenge, especially in the face of degenerative or progressive arthropathies, behavioral science