Dear Reader,

We are happy to present the sixth issue of the ‘Press Review and Journal Club’ newsletter that is part of a EULAR School of Rheumatology (ESOR) educational initiative, the EULAR-EMEUNET Journal Club. This newsletter includes an overview of relevant articles published both in top rheumatology journals and in major internal medicine journals during the last 4 months (September-December 2018). The article selection includes translational and clinical research papers; in case you want to read the article in more detail, a hyperlink will redirect you to the respective journal. Among the selected articles, one has been chosen by the ESOR faculty to be discussed in a few weeks in an online Twitter Journal Club. Another article, the ‘EMEUNET Paper of the Month’ has been selected by popular vote through a survey circulated among the rheumatology community. For the latter, a video interview with the first author explaining the main findings of the paper is available on our YouTube channel.

The Journal Club aims to bring together rheumatologists, clinical researchers, basic scientists, and anyone else who might be interested in the topic, to participate in an online, lively discussion. These ‘meetings’ take place on Twitter at pre-specified times and dates; the next is planned on February 6th at 8:30 PM GMT (9:30PM CET). ‘Save the date’ reminders will be sent in advance. Where possible, key authors involved in selected articles will be invited to participate. The selected article will be freely accessible for a limited period of time on the journal website. Details of the article selected and of the Journal Club are included on pages 3 and 4 of this issue.

We hope that you will enjoy reading this newsletter and look forward to ‘seeing’ you soon at our Twitter JC meeting!

Paul Studenic, Richard Conway, Alessia Alunno, Elena Nikphorou, Antonis Fanouriakis, Achilleas Floudas, Chris Wincup, James Bluett, Sarah Wade and Mikhail Protopopov, on behalf of the EULAR EMEUNET Journal Club team

**JAK/STAT Blockade Alters Synovial Bioenergetics, Mitochondrial Function, and Proinflammatory Mediators in Rheumatoid Arthritis**


Pannus formation in rheumatoid arthritis is characterized by a metabolic shift due to O$_2$ consumption and a hypoxic microenvironment within the synovium. Evidence suggests that the JAK-STAT signaling pathway may be involved in regulating metabolic pathways in synovial cells. The authors aimed to explore the mechanistic effects of tofacitinib, a JAK-STAT inhibitor approved for RA, on synovial fibroblast cells of patients with the disease. They found that tofacitinib significantly decreased mitochondrial membrane potential, mass and ROS production by RA fibroblasts, and altered the expression of key mitochondrial genes. Specifically, it restored metabolic homeostasis, by significantly increasing oxidative phosphorylation, ATP production and respiratory performance, with a parallel decrease in anaerobic glycolysis. These data support that JAK-STAT signaling may mediate the complex interplay between inflammation and cellular metabolism in RA pathogenesis.

The online Journal Club will take place on:

**Wednesday 6th February 2019 at 8:30PM GMT (9:30PM CET)**

- **duration 1 hour**-

Follow the accounts [@EULAR_JC](#), [@eular_org](#) and [@EMEUNET](#)

Use the hashtag #EULARJC to follow and join the discussion

Trimethoprim–sulfamethoxazole prophylaxis prevents severe/life-threatening infections following rituximab in antineutrophil cytoplasm antibody-associated vasculitis


Antineutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV) are accompanied by significant morbidity and mortality. With improvements in prognosis, comorbidities due to persistence of the disease or side-effects of therapy remain a major challenge. Most deaths in the disease course are caused by infections. Kronbichler et al aimed to assess risk factors for the development of severe infections in 192 patients with AAV following treatment with rituximab (RTX). Overall severe infection rate was 26.06/100 person-years. By performing univariate and multivariable analyses, the authors found that prophylactic use of trimethoprim–sulfamethoxazole (which was administered in 38% of patients) was associated with a significantly lower frequency of severe infections (HR 0.30, 95% CI 0.13-0.69); on the contrary, older age, endobronchial involvement, presence of chronic obstructive pulmonary disease and previous alemtuzumab use increased the respective risk. These observations may have obvious implications for the routine management of AAV patients, in order to minimize the risk for infections.

Explore this paper in greater detail through an exclusive interview with study first author ...

Interview available here

The EMEUNET Paper of the Month is selected by an online vote of selected articles from each of the rheumatology journal contributions.

Watch out for our next poll!
ANNALS OF THE RHEUMATIC DISEASES

Volume 77 Issues 9-12

Achilleas Floudas and James Bluett

Achilleas is currently working in the Molecular Rheumatology lab of Prof. Ursula Fearon at Trinity College Dublin, Ireland. He completed his undergraduate Biology studies at the University of Crete, Greece, and received a PhD by the Institute of Molecular Medicine of Newcastle University, UK. His research is currently focusing on the role of T and B cells at the site of inflammation in rheumatoid arthritis, and the effect of hypoxia on the function of these cells. Achilleas is a member of the Newsletter Subgroup.

James is a senior clinical lecturer, honorary consultant in rheumatology and co-deputy director of the MSc “Clinical rheumatology” at the University of Manchester, UK, with an interest in strategies to improve treatment response in rheumatoid arthritis (RA). In 2015, he completed a PhD exploring methotrexate adherence in RA and methotrexate-pneumonitis. James is a member of the Newsletter Subgroup.

Systemic lupus erythematosus (SLE) is characterised by the production of autoantibodies and immune-complex glomerulonephritis. Ma et al (pp 1498-1506) characterized a novel TLR4+ CXCR4+ population of plasma cells (PC) which are increased in peripheral blood and renal tissue of SLE patients. Using an adoptive transfer mode, the authors showed that transfer of TLR4+ CXCR4+ PC led to autoantibody production and development of glomerulonephritis in recipient mice. Importantly, TLR4 inhibition resulted in reduced autoantibody production in vitro and reduced renal damage in vivo. Synovial inflammation in rheumatoid arthritis (RA) is potentially driven by activated, inflammatory synovial fibroblasts (SF). Neumann et al (pp 1619-1626) explored the potential contribution of SF CD82, a multifunctional membrane adaptor with previously shown roles in signal transduction and cell motility, in the pathogenesis of RA. RA-SF CD82 expression is upregulated by pro-inflammatory cytokines, commonly found in the inflamed joint, with low CD82 expression leading to high SF migratory capacity and otherwise, proposing that CD82 is an important mediator of SF migration to sites of inflammation while CD82 overexpression can cause on site entrapment of inflammatory SF. Pathogenic T follicular helper (Tfh) cells can mediate autoimmunity by their contribution of pro-inflammatory cytokines and help provided to autoreactive B cells. A subpopulation of Th1 like Tfh cells has previously been associated with Systemic lupus erythematosus (SLE) pathogenesis. Ma et al (pp 1354-1361) showed IL-12 mediated activation of STAT1 and STAT4, which in turn bind the transcription factors BCL6 and TBX21 leading to increased generation of Tfh-Th1 cells. Serum levels of IL-12 and peripheral blood Tfh-Th1 cells were increased in SLE patients compared to healthy controls. It has previously been shown that mast cells can lead to B cell activation and increased antibody production. Rivellese et al (pp 1773-1781) report a significant positive correlation between mast cell and B cell numbers in the synovial tissue of treatment-naïve patients with early rheumatoid arthritis (RA), while coculture of peripheral blood derived mast cells and peripheral blood B cells led to increased B cell survival and enhanced class switch recombination resulting in increased IgG production. Interestingly, in Il27ra deficient mice there is enrichment in synovial mast cells and increased tissue damage. Hand osteoarthritis (hOA) is a prevalent disease with limited treatment options. In a study including 90 patients, Kloppenburg et al (pp 1757-1764) showed that etanercept did not relieve pain in patients with symptomatic inflammatory erosive hOA compared to placebo (the mean between-group difference in VAS pain at 1 year was -8.5 (95% CI -18.6 to 1.6) favouring etanercept.
Methotrexate is one of the first-line csDMARDs for patients with rheumatoid arthritis (RA) and early treatment response is essential to prevent joint damage. Teitsma et al (pp 1261-1267) investigated predictors of methotrexate response using data from the U-ACT-EARLY, a 2-year randomised clinical study evaluating disease remission (DAS≤2.6) in newly diagnosed RA patients. Oral methotrexate was started at 10mg/week and increased up to 30mg/week until remission or maximal tolerated dose. If remission was not achieved, hydroxychloroquine was added by week 20, followed by tocilizumab at week 32. 48% of patients achieved remission without the need for tocilizumab at year 1. Baseline DAS28 (adjusted OR 2.1, 95% CI 1.4 to 3.2) and current smoking (adjusted OR 3.02, 95% CI 1.1 to 8.0) were predictors of inadequate response (defined as unable to achieve remission to methotrexate plus hydroxychloroquine, adverse event or inefficacy) at 1 year. ANCA-associated vasculitis (AAV) is a group of small to medium vessel vasculitis leading to organ failure and death. Rituximab in combination with glucocorticoids is used for induction of remission. Despite the risk of life-threatening infections, no antibiotic guidelines currently exist for patients receiving rituximab. Kronbihler et al (pp 1440-1447) investigated risk factors for severe infections in patients with AAV. 192 Patients who received rituximab were recruited over a 10 year period. Approximately 25% of patients developed severe infections. Prophylactic trimethoprim–sulfamethoxazole significantly reduced the risk of developing severe/life-threatening infections by 70% and reduced the time to first significant infection.

Despite a number of treatment options existing for patients with rheumatoid arthritis (RA), finding the right treatment for the right patient is still trial and error. Kearsley-Fleet et al (pp 1405-1412) investigated the frequency and predictors of bDMARD refractory disease from the British Biologics Register. Over 111,034 person-years of follow-up, 6.4% patients experienced refractory disease requiring at least three different classes of bDMARDs. In the multivariable analysis, recent registration, female sex, younger age, shorter disease duration, higher baseline global assessment, higher HAQ levels, smoking, obesity and greater social deprivation were associated with refractory disease. Despite showing a good effect in psoriatic arthritis, anti-IL-23 antibodies failed to show a significant clinical efficacy in patients with ankylosing spondylitis (AS, also known as radiographic axial spondylarthritis, r-axSpA). Baeten et al. (pp 1295-1302) reported that IL-23 inhibitor risankizumab showed no evidence of clinically meaningful improvements compared with placebo in patients with active AS in a stage 2 clinical study including 59 patients with biological-naïve AS (ASAS40 response rates 25.5%, 20.5% and 15.0% in the 18 mg, 90 mg and 180 mg risankizumab groups, respectively, compared with 17.5% in the placebo group).
JAK/STAT mediates the complex interplay between inflammation and cellular metabolism in rheumatoid arthritis (RA) pathogenesis. Using synovial explants, synovial fibroblasts, seahorse technology and mitochondrial assays, McGarry et al (pp 1959-1970) identified a beneficial metabolic effect of JAK/STAT inhibitor Tofacitinib in RA: it has significantly decreased reactive oxygen species production and glycolysis rates in RA synovial fibroblasts, with parallel decrease of key metabolic enzymes and pro-inflammatory mediators including HK2, lactate dehydrogenase, IL6 and IL8. Ciccia et al (pp 2003-2013) examined the frequency and function of CX3CR1+ mononuclear phagocytes (MNPs) in ankylosing spondylitis (AS/raxSpA). MNP populations producing high levels of TNF-like molecule 1A and IL23 were expanded in the gut of AS patients compared to healthy control counterparts. Isolated MNPs promoted the expansions of gut-derived innate lymphoid cell 3 (ILC3), cells previously associated with AS pathophysiology, suggesting a feed-forward chronic inflammatory loop. In peripheral spondyloarthritis (pSpA), Van Mens et al (pp 1994-2002) characterised the effect of a 12-week anti-IL17 treatment on the synovial immunopathology. Synovial immunohistochemistry revealed a significant decrease in neutrophils (CD15) and macrophages (CD68) in secukinumab-treated patients. Further molecular analysis identified a significant reduction in key pro-inflammatory mediators including IL-17A, IL-6 and MMP3. Taken together, these data support a significant immunopathologic impact of anti-IL17 treatment on pSpA. Watanabe et al (pp 1626-1633) investigated the link between the reappearance of myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) and relapse in ANCA-associated vasculitis. In a cohort study, the authors measured MPO-ANCA levels at 0, 3, 6, 12, 18 and 24 months and at the time of relapse. Of the 271 patients recruited, MPO-ANCA levels normalised within 6 months in 72% of cases. Reappearance of the antibody was more frequent in patients with a relapse. Emmi et al (pp 1500-1507) evaluated the clinical efficacy and steroid-sparing capacity of adalimumab against csDMARD therapy in Behçet’s syndrome (BS)-associated venous thrombosis in a retrospective study of 70 patients with venous complications of BS. In those treated with adalimumab, both clinical and imaging improvement of thrombosis was seen more often than in those on csDMARDs. Lovell et al (pp 1508-1518) explored the risk, time and predictors of flare after anti-TNF therapy discontinuation in children with polyarticular juvenile idiopathic arthritis (JIA). The study recruited 137 patients with clinically inactive JIA for at least 6 months and assessed for time to flare in those discontinuing anti-TNF therapy. More than one-third of patients with sustained inactive disease flared within 8 months of stopping anti-TNF therapy. Patients with a short disease duration and older age of onset were less likely to flare.
Van der Meulen et al (pp 2225–2234) examined the buccal bacterial composition of 37 patients with primary Sjögren’s syndrome (SS) compared to 67 non-SS patients with similar symptoms and 24 healthy controls. The authors reported elevated ratios of Firmicutes/Proteobacteria in SS and non-SS compared to the healthy control counterparts. Interestingly, only two bacterial subclasses were distinct in SS compared to non-SS, suggesting a similar dysbiosis of the buccal mucosa microbiome in SS and symptom control non-SS patients. Using a collagen-induced arthritis model (CIA), Jordan et al (pp 2042–2052) reported the importance of osteoclast-associated CCL3 in bone loss and erosion. In vitro, neutralisation of CCL3 significantly reduced osteoclastogenesis and re-absorption of bone substrates. In CIA, CCL3 blockade reduced joint damage in the wrists and elbows, while also reducing joint-associated osteoclasts in the hind and fore paws. Van den Hoogen et al (pp 1669–1674) investigated the role of post-transcriptional regulators, microRNA, in plasmacytoid dendritic cell (DC) activation in systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS). While there was no significant difference in microRNA expression in DCs isolated from patients with SLE and ALS, miR-35, 17 and 21 were significantly decreased in SLE and ALS compared to healthy controls. By comparing low versus high interferon signatures, the authors also identified an association between lower miR-361-5p, miR-128-3p and miR-181a-2-3p expression and high interferon signatures suggesting microRNA induced-DC dysregulation in SLE and ALS. A prospective study by Ehrenstein et al (pp 1592–1601) assessed the ability of rheumatologists to correctly identify patients with and without rheumatoid arthritis (RA) when blinded to prior workup. It was found that the correct diagnosis based on clinical assessment alone improved from 27% to 53% with the inclusion of ultrasonographic assessment, and to 70% after laboratory investigations were also taken into account. The study concluded that if deprived of imaging and laboratory investigations even experienced rheumatologist will find it difficult to make a diagnosis of RA based on a brief symptom-focused history and physical examination alone. Novikov et al (pp 2101–2105) reviewed the efficacy of Certolizumab pegol in the treatment of ten female patients of reproductive age with Takayasu arteritis (TA). The case series found the treatment leading to rapidly induced and maintained remission in 9 of the 10 patients. It was concluded that Certolizumab pegol could be considered in female patients with TA considering pregnancy.
Immune complexes (IC) are a characteristic of **systemic lupus erythematosus (SLE)**. Endogenous RNA and DNA can be trapped by IC, by internalising IC, plasmacytoid dendritic cells (pDC) can be exposed to the trapped nucleic acids leading to activation of TLR-7 and TLR-9, respectively. Hjorten et al (20:238) assessed how an interleukin (IL)-1 receptor-associated kinase 4 small molecule inhibitor (IRAK4i) can alter pDC and natural killer cell cytokine production following internalisation of IC. Interestingly, IRAK4i altered RNA-IC induced gene expression and resulted in reduced pro-inflammatory cytokine production by both pDC and natural killer cells. Barbati et al (20:273) explore the potential contribution of microparticles - small membrane vesicles with a 0.1 to 1.0 µm diameter, previously shown to be increased in the periphery of RA patients - in pathogenesis of **rheumatoid arthritis (RA)**. MP were isolated from healthy individual’s and RA patient’s peripheral blood and their contribution to apoptosis and autophagy of endothelial cells was assessed. MP of RA patients were decorated with TNF-a and could cause increased apoptosis and autophagy of endothelial cells. A significant positive correlation between MP TNF-a and DAS28 score for RA patients was shown (r=0.4, p=0.01). Arevalo et al (20:221) investigated the influence of HLA-B27 on the clinical phenotype of **ankylosing spondylitis (AS)/axSpA** using data from the observational Spanish REGISPONSER database. They showed that in Caucasian AS patients HLA-B27 is associated with younger age at diagnosis (OR 0.97, 95% CI 0.96–0.98) and that HLA-B27 poresize was less likely associated with peripheral arthritis (OR 0.53, 95% CI 0.32–0.89), dactylitis (OR 0.16, 95% CI 0.05–0.56), psoriasis (OR 0.45, 95% CI 0.26–0.78), and IBD (OR 0.22, 95% CI 0.12–0.40). Kawashiri et al. (20:277) identified fibrosis-related serological surrogate outcome measures in patients with **im munoglobulin G4-related disease (IgG4-RD)**. In a clinical observational study of 72 patients with untreated IgG4-RD and 44 healthy controls, the serum concentrations of growth differentiation factor 15 (GDF-15) were independently associated with the presence of retroperitoneal fibrosis (OR 3.47, 95%CI 1.2–11.4) and with parotid gland involvement (OR 3.92, 95% CI 1.0–19.5), although not not associated with the IgG4-RD RI score or the number of organ involvements). Roughley et al. (20:243) quantify the risk of chronic kidney disease (CKD) stage ≥ 3 in people with **gout** and the impact of urate-lowering therapy (ULT) in a retrospective cohort study using data from the Clinical Practice Research Datalink and including including 41446 patients with incident gout matched to patients without gout. Gout was associated with an increased risk of incident CKD (adjusted HR 1.78 95% CI 1.70 to 1.85). In those exposed to ULT, the risk of incident CKD was generally comparable with the matched controls.
In recent years, an increased incidence of chronic inflammatory arthritis associated with Chikungunya infection has been reported. A systematic review by Amaral et al (pp. 1501-1508) that identified 6 studies concluded methotrexate to be an effective treatment for **Chikungunya arthritis**. The authors conclude that a detailed prospective randomised controlled trial is needed. In a large scale global inception study of 1,826 patients with **systemic lupus erythematosus (SLE)**, Hanley et al (pp. 1478-1487) evaluated the prevalence, characteristics and clinical outcomes of patients with cerebrovascular events (including stroke, transient ischaemia, chronic multifocal ischaemia, subarachnoid/intracranial haemorrhage and sinus thrombosis). The study found that these events accounted for the fourth most frequent neuropsychiatric manifestations of the disease - 82 of 1826 patients had 103 events that were attributed to SLE. Interestingly in spite of good physician-reported outcomes, patients described significant reduction in quality of life following the event. A study by Arora et al (pp. 1771-1777) aimed to compare the differences in the quality of care in patients with **systemic lupus erythematosus (SLE)** attending a dedicated lupus clinic and those being treated in a general rheumatology clinic. The findings support the use of dedicated specialist lupus clinics, in which patients were more likely to be given counselling regarding sunscreen use (98.7% and 83.6%, respectively; p=0.001), screened for antiphospholipid syndrome (71.4% and 37%; p<0.001), be on steroid-sparing agents (100% and 82%; p<0.007) and undergo regular bone mineral density testing (94.2% and 54.5%; p<0.001).

The clinical characteristics and factors associated with disability and reduced quality of life in children with **juvenile systemic sclerosis (JSS)** were assessed by Stevens et al (pp. 1806-1813). In a study of 64 patients recruited from the multinational Childhood Arthritis and Rheumatology Research Alliance Legacy Registry, the authors highlighted that multiorgan manifestations were common and functional disability was higher than in other childhood-onset rheumatic diseases - in 38% of patients, ≥4 organ systems were affected. In particular, gastrointestinal manifestations of the disease were reported to confer the greatest impact on quality of life. In **idiopathic inflammatory myopathy (IMM)**, the incidence of venous thromboembolic events was investigated by Antovic et al (pp. 1849-1855). The study utilised national registry data to compare the rates of venous thromboembolism (VTE) in IMM and in general population. Authors conclude that rates of VTE were higher in those with IMM (HR 7.81, 95%CI 4.74 to 12.85) compared to general population. and those with a history of cancer (HR 21.80, 95%CI 2.63 to 180.75) and aged >71 years at the time of the diagnosis (HR 5.46, 95%CI 2.57 to 11.61) were of highest risk. Furthermore, those with dermatomyositis were found to be of greater risk.
In a study of 152 patients with low disease activity rheumatoid arthritis (RA) (defined as a DAS<3.2), Bechman et al (pp 1515-1521) demonstrated that flares (an increase in DAS28 compared with baseline of > 1.2, or > 0.6 if concurrent DAS28 ≥ 3.2) are common with 30% experiencing a flare within the one year of study period. Those who suffered from flares were more likely to have erosive progression and worse quality of life. The authors highlight that flares in low disease activity associated with poor clinical outcome. McCulley et al (pp 1636-1642) investigated the association between medication beliefs and adherence to therapy in a diverse cohort of patients with rheumatoid arthritis (RA) with from the USA. Using telephone based interviews, 362 patients were recruited of which 14% self-reported poor adherence to oral DMARDs/prednisolone whilst 21% described poor adherence to biologics. It was suggested that patients with stronger beliefs regarding the necessity of treatment were more likely to have better adherence with oral therapy. Interestingly, higher self-efficacy was associated with poorer adherence. T cell apoptosis is considered to be one of the key pathogenetic mechanisms in systemic lupus erythematosus (SLE). Xie et al (pp 1397-1405) reported decreased expression of miR-98 in SLE peripheral CD4+ T cells, levels of which were associated with increased mRNA and protein levels of apoptosis regulator, FAS. Inhibition of miR-98 in healthy T cells resulted in a SLE-like pro-apoptotic phenotype, while enhanced expression of miR-98 effectively reversed the phenotype. In a retrospective study of 16 patients with systemic lupus erythematosus (SLE) and class III/IV/V nephritis, sirolimus was suggested as an alternative therapy in those who could not tolerate standard treatment or had a history of malignancy. Yap et al (pp 1663-1670) found sirolimus effective when used in combination with corticosteroids without excessive side effects. The role of faecal calprotectin in the detection of inflammatory bowel disease in patients with juvenile idiopathic arthritis (JIA) was assessed by Ferrara et al (pp 1418-1421). In a study of 113 patients, 7 were noted to have raised calprotectin levels (all had inflammatory bowel disease). In 3 cases raised calprotectin was the only sign of bowel disease. Cheng et al (pp 1696-1704) examined the relationship between angiogenesis and bone health in osteoporosis. Expression levels of angiogenic markers, VEGF, ANG1, ANG2 were significantly lower in endothelial progenitor cells isolated from patients with osteoporosis compared to healthy control comparators. Lower angiogenic factors were negatively associated with decreased bone mineral density of total hip and femoral neck.
The gene TNFAIP3 encodes A20, a negative regulator of NF-κB activation. Previous studies have demonstrated polymorphisms of TNFAIP3 are associated with auto-inflammatory disorders. In their study, Rajamäki et al (e000740) describe a novel loss of function mutation of TNFAIP3 and raise the question whether polymorphisms of TNFAIP3 could be a confiding factor in the pathogenesis of rheumatic diseases. In haploinsufficient individuals, the authors report increased NLRP3 inflammasome activation and increased IL-1β and IL-18 secretion. The clinical course of axial spondyloarthritis (axSpA) is heterogeneous. Imkamp et al (e000755) were able to identify 5 typical trajectories of health-related quality of life disease activity in axSpA, using the data of the OASIS cohort, and to identify baseline characteristics of patients associated with these trajectories. For example, the trajectory of low impact of the disease showed the largest proportion of males and HLA-B27 carriers, and the trajectory very high impact of disease was represented by the highest proportion of females. Inflammatory back pain (IBP), the key symptom of axial spondyloarthritis (axSpA), has been proposed as a screening test for patients presenting with chronic back pain in primary care. Poddubnyy et al. (e000825) checked its diagnostic accuracy in the rheumatology setting. The sensitivity of IBP according to various definitions was comparable to published figures in the primary settings, whereas the specificity (and, therefore, the resulting positive likelihood ratios) were unexpectedly low with no significant difference between different sets of IBP criteria. However, this was counterbalanced by a high prevalence of IBP among referred patients, suggesting that the awareness of the IBP criteria by primary care specialists and the effective use of IBP as selection parameter for referral was the reason of such discrepancies. Lauper et al (e000809) analyzed the data from 8 European registries to compare the real-word effectiveness of subcutaneous and intravenous tocilizumab in rheumatoid arthritis (RA). Similar retention rates and effectiveness were seen in both groups. Fragoulis et al. (e000739) reported the rate of neutropenia, a recognised finding in the context of rheumatoid arthritis (RA) often linked to treatment with DMARDs, in patients with newly diagnosed RA from the Scottish Early Rheumatoid Arthritis inception cohort. Neutropenia episodes were recorded 7.5% patients with RA at a median of 12 months after RA diagnosis, and was not related to a certain DMARD (rates were 4.92, 6.68 and 5.69 per 1000 persons-months for methotrexate, sulfasalazine and hydroxychloroquine). Patients who developed neutropenia were more likely to be female (p=0.01) and non-smokers (p=0.007) and had lower baseline neutrophil levels (p<0.0001).
Sumida et al (Nature Immunology, 19:1391–1402) describe a novel mechanism that connects environmental factors to Treg cell dysregulation and autoimmunity. Dysregulated Treg cell responses have been implicated in a plethora of autoimmune conditions. An imbalance between Treg cell pro-inflammatory IFN-γ and anti-inflammatory IL-10 production has been previously associated with the development of Multiple Sclerosis. The authors, through RNA-sequencing of human Treg cell populations, reveal β-catenin as a key mediator of an imbalanced, dysfunctional Treg cell cytokine responses characterised by increased IFN-γ production that could promote autoimmunity. By utilising fate mapping, Fang et al (J Exp Med, 215:2705-2714) in their study show that T follicular helper cells (Tfh) that produce IFN-γ have, at some earlier point in their development, undergone a transient expression of the transcription factor T-bet. These ex-Tbet Tfh cells have the capacity to produce IFN-γ at germinal centres in vivo and thus influence B cell class switch recombination towards specific Ig subtypes. This is the first study that describes that transient T-bet expression by Tfh cells is adequate to invoke sustained IFN-γ production and can influence our understanding of Th1 and Tfh responses. Hyperuricaemia is a major risk factor for the development of gout. Eating red meat, shellfish, alcoholic drinks, sugary drinks and tomatoes have been linked with increased serum urate levels. Major et al (BMJ, 363:k3951) conducted a meta-analysis of food frequency questionnaire data from five US cohort studies to evaluate the association and contribution of particular foods with serum urate. Their findings replicated and discovered new associations between foods and raised serum levels (replicated: beer, spirits, wine, poultry, soft drinks and meat. New associations: potatoes) and eight foods with reduced serum urate levels (replicated: eggs, cold cereal, skimmed milk, cheese, brown bread and non-citrus fruit. New associations: peanuts and margarine). Authors demonstrated however that the diet alone explains only a small amount of variation in serum urate (≤0.3%) compared to common genetic variants (23.9%). This study provides evidence that the development of hyperuricaemia is, for the most part, not affected by diet. Anti-IL-17 antibodies, namely secukinumab, have already shown their effectiveness in ankylosing spondylitis (AS/r-axSpA). Van der Heijde et al. (Lancet, 392:2441-2451) reports that another anti-IL-17A inhibitor, ixekizumab, which is already registered for the treatment of psoriasis and active psoriatic arthritis, was efficacious in the treatment of AS with significant improvements in disease activity, health-related quality of life, physical activity and bone marrow oedema of the spine and sacroiliac joint in patients previously untreated with bDMARDs, and non-inferior to adalimumab.
EDUCATIONAL EVENTS

JANUARY 2019

EULAR Endorsed Course: Sonoanatomy 11 Shoulder + Ligaments

• When and Where: 24 – 25 Jan 2019, Barcelona, Spain

FEBRUARY 2019

14th Annual Biomarkers Congress
• When and Where: 21 - 22 Feb 2019, Manchester, UK
• Website: https://www.oxfordglobal.co.uk/biomarkers-congress/

1st Immunology and Inflammation (I&I) Conference
• When and Where: 24 - 26 Feb 2019, Berlin, Germany
• Website: https://www.mdc-berlin.de/immunology-inflammation-2019

39th European Workshop for Rheumatology Research (EWRR)
• When and Where: 28 Feb – 2 Mar 2019, Lyon, France
• Website: http://www.ewrr.org
The European Workshop for Rheumatology Research (EWRR), is the premier annual event in Rheumatology Research in Europe. It takes place every year since 1981 in a European country. In an intense 2.5 day meeting of 250-300 selected junior and senior researchers, cutting edge work on rheumatology and inflammation is presented, new collaborations are established, networking is facilitated and partnership with other biomedical fields and the industry is promoted. In short, this is the top rheumatology research meeting in the world with a local European flavor.

From the message of the organizer, Pierre Miossec:

“As always, the topics cover the whole field of rheumatology research from basic to translational aspects leading to better care. The 2019 meeting will focus on IL-17 and IL-17 producing cells, cell-cell interactions at the disease site, the systemic effects of inflammation. In keeping with the principle of pushing the young up, many opportunities will be given to the young to discuss their results for oral presentation, during poster tours, and breakfast discussions with the more mature on career opportunities.”

The 39th EWRR Meeting will take place on 28 Feb - 2 March 2019, in Lyon, France

For more information, visit: http://www.ewrr.org
EULAR IMAGING COURSE

For Rheumatology trainees and Rheumatologists, this is a comprehensive new course on conventional radiography, magnetic resonance (MR), computerized tomography (CT) and ultrasonography (US).

The course will further focus on lectures and workshops. The lectures will convey the possibility of questions and interactive discussion with the faculty in the end. The workshops will consist of interactive learning and practical training, discussing clinical cases and images (some of which selected from participant’s applications). This is a compact, two-day imaging course with a focus on conventional radiography, computed tomography, magnetic resonance imaging and ultrasound.

The lectures will convey the possibility of questions and interactive discussion in the end. The workshops will consist of interactive learning and practical training, which will last at least one hour. Applicants will be divided into 3 classrooms where they can present their cases / images and discuss it with the faculty and other applicants. Moreover, the faculty will present images and provide practical training in the interpretation of the different imaging modalities.

There will be 5 workshops: one for peripheral radiography, one for axial radiography, one for axial and peripheral MRI, one for CT scan and one for ultrasonography interpretation.

Registration requires participants applying for the course to send 3 radiography pathology images, 2 MR pathology images, 1 CT scan pathology image and 2 ultrasound pathology images.

The EULAR Imaging Meeting will take place on 28-30 March 2019, in Amsterdam, The Netherlands

EULAR grants 5 bursaries of EUR 500 each for applicants below the age of 40 at the time of application.

For information, visit: https://esor.eular.org/theme/lc_eular/layout/enrol.php?id=16
JOIN EULAR TASK FORCES AND COMMITTEES

Young investigators of EMEUNET are an integral part of all task forces and committees working on new EULAR recommendations. This is a wonderful chance for EMEUNET to increase its visibility and for you to accelerate your academic career.

EMEUNET members with interest in methodology and previous experience in EULAR Task Forces can also have the opportunity to become junior methodologists. For further information, please contact emeunet.education@gmail.com

Take a look at emails from EMEUNET and find the opportunity most suitable for you!

SHARE YOUR IDEAS!

Over the years EMEUNET has developed several projects covering different topics and areas of interest. However, we appreciate any suggestions and welcome new ideas to expand on what we currently offer to EMEUNET members. Make your voice heard and share your ideas with us!

It is easy, just write down some lines to summarize your proposal and send it either via email at emeunet@eular.ch or through our website (http://emeunet.eular.org/contact_us.cfm). Don’t forget to provide your contacts so we can come back to you for additional details!

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