The 12th Medinterna International Meeting took place in Porto, Portugal, from 27 February to 1 March 2014. This annual conference is organized by the Medinterna Association and sponsored by São João Hospital Centre. Different topics in Autoimmunity were discussed over the three days.

The first day of the meeting, 27 February, was dedicated to arthritis, specifically rheumatoid arthritis, risk cardiovascular factors in RA, and the relationship between bone, cartilage and osteoporosis.

**WHAT DID WE LEARN ON FEBRUARY 27?**

Vasculitis was the theme of the first morning of the meeting. João Viana (Lisbon, Portugal) spoke about the variability in autoantigens, antibodies and measurement tests, resulting in conflicting laboratory results in autoimmunity. The need for standardization and uniformity of these tests to help clinicians in daily practice was also reinforced.

The subject of the second session was pulmonary involvement in sarcoidosis. Athol Wells (London, UK) talked about the lack of understanding of treatment goals in this disease and the difficulty to predict which patients will progress to severe disease. The main treatment indications were noted, as was the unacceptable loss of quality of life and the danger of long-term disability.

Yehuda Shoenfeld (Tel Aviv, Israel) talked about vitamin D as an immunomodulating agent in autoimmune diseases. Several studies have demonstrated the association of vitamin D deficiency, infections and autoimmune diseases. However, discussion was centered on the hypothesis that low vitamin D is a result of the disease and not a cause itself, serving as a biological marker more than a therapeutic one.

The subject of the next two sessions was Sjögren syndrome. Jan Damoiseaux and Jan Willem Cohen Tervaert (Maastricht, The Netherlands) used a clinical case to exemplify the changes in classification criteria in this syndrome, with special attention to the antibodies. The importance of the antibodies in pregnancy leading to two major complications, neonatal systemic lupus erythematosus and congenital heart block, was emphasized. Cees Kallenberg (Groningen, Netherlands) reviewed the biological therapeutic tools in Sjögren syndrome, presenting several studies that used rituximab, epratuzumab, belimumab and abatacept with promising results.

The afternoon proceeded with Bruno Vidal and Diana Fernandes (Lisbon, Portugal) presenting some preliminary results of their work on nano-inflammation. Animal models of arthritis were used to prove the role of cytokines implicated in this disease in bone structure and in atherosclerosis.

Monika Ostensen (Kristiansand, Norway) highlighted the importance of adequate contraception and pregnancy planning in patients with rheumatic diseases, discussing the need for risk stratification in these patients according to disease activity and antibodies. The contraindications of some drugs in pregnancy were also reviewed, including those that are not used due to lack of knowledge or because of proven teratogenicity.

After a brief revision of thrombocytopenic idiopathic purpura, Ducla Soares (Lisbon, Portugal) spoke about the paradigm shift in diagnosis and treatment. Attention was focused on the importance of decreased platelet production in the pathogenesis of this disease as well as on the thrombopoietin analogues as promising therapeutic targets.

The next subject, presented by Carlo Perricone (Rome, Italy), was ASIA syndrome, an autoinflammatory syndrome induced by adjuvants. He discussed the current data which support the role of various environmental factors in the pathogenesis of immune mediated diseases. Some examples were given, such as Gulf War syndrome, siliconosis and post-vaccination syndrome.

Pedro Vita (Porto, Portugal) concluded the first day of the meeting with a talk on RA treatment, with particular emphasis on interleukin-6 inhibition with tocilizumab. Some studies demonstrating the superiority of tocilizumab in monotherapy and in controlling systemic manifestations of the disease were presented.

**WHAT DID WE LEARN ON FEBRUARY 28?**

Systemic sclerosis was the topic of the morning and part of the afternoon. Luc Mouthon (Paris, France) focused on muscle involvement in Systemic sclerosis (SSc), naming the three components that are responsible for its pathogenesis: vascular hyperreactivity, fibrosis, and autoantibodies. Skeletal involvement in SSc is frequent, but often mild and related to diffuse cutaneous...
SSc and anti-PM/Scl antibodies. Whenever skeletal muscle is involved, cardiomyopathy must be excluded. Moreover, muscle biopsy is warranted not only for diagnostic purposes but also for prognosis, since inflammation and necrosis predict response to treatment, while patients with non-inflammatory myopathy should not be treated with steroids.

Bodo Grimbacher (London, UK) spoke of the high prevalence of autoimmunity in patients with primary immunodeficiencies and that this immune dysregulation may manifest only during adulthood. LRBA mutations occur in common variable immune deficiency, establishing a possible link between autoimmunity and autophagy. On the other hand, autoimmune polyendocrine syndrome type 1 was mentioned to illustrate the role of cell cytokines in fungal control.

At the roundtable of the day, activity markers of SSc were discussed. Ignacio Martin Suárez (Huelva, Spain) listed which biomarkers are being considered in SSc and highlighted the need for validated biomarkers for diagnosis, disease classification and evaluation of organ involvement and therapeutic response. Isabel Almeida (Porto, Portugal) explained how activity can be evaluated in cutaneous and articular involvement, using tools as the durometer, the modified Rodnan skin score, ultrasonography or magnetic resonance imaging. Maria Jesús Castillo Palma (Sevilla, Spain) did the same for cardiopulmonary involvement, pointing out that damage occurs early in SSc and that lung and heart involvement are the major causes of SSc-related deaths.

Carlos Aguiar (Lisbon, Portugal) presented atherosclerosis as an inflammatory disease, emphasizing that the management of autoimmune diseases should address global cardiovascular risk since it may reduce coronary artery disease and potential morbidity. Examples were also given of how cardiovascular risk is increased in disorders such as psoriasis, RA or SLE.

Cândida Abreu (Porto, Portugal) talked about infection and vaccination by zoster virus in the elderly and in autoimmune diseases and showed how the number of specific memory T cells decrease with age below a threshold, which represents a significant risk for zoster infection. The complications of zoster infection were listed, and preventing infection through vaccination in patients aged 60 years or older was recommended.

After lunch, Ivone Silva (Porto, Portugal) described which risk factors are consistently associated with the development of digital ulcers [Table 1], the role of angiogenesis biomarkers, and how nailfold videocapillaroscopy patterns and scores may be used as an outcome measure. The treatment of digital ulcers was highlighted, through pain management, antibiotics, vaso-dilatation, tissue repair, iloprost for active ulcers, and either bosentan or iloprost for ulcer prevention.

Rui Baptista (Coimbra, Portugal) reinforced the idea that current available therapies for pulmonary hypertension are effective even in mildly symptomatic SSc patients; screening algorithms were explained in general, including the DETECT study which is a sensitive, non-invasive tool for detection of PAH. It should be remembered that all patients with SSc need to be screened for PAH which, if detected, will require right heart catheterization.

The rest of the afternoon was dedicated to antiphospholipid syndrome and SLE. Jo Berden (Nijmegen, The Netherlands) summarized the role of nucleosome as the driving autoantigen in SLE and how binding mechanisms occur. In clinical practice, anti-nucleosomes are more sensitive than anti-dsDNA with equal specificity, and the presence of nucleosome/autoantibody complexes is associated with the onset and exacerbations in lupus nephritis.

### Table 1. Risk factors for digital ulcers in SSc

<table>
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<tr>
<th>dSSc</th>
<th>Male</th>
<th>Scl70</th>
<th>Early age at RP onset</th>
<th>ESR</th>
<th>Pulmonary disease</th>
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dSSc = diffuse systemic sclerosis, RP = Raynaud’s phenomenon, ESR = erythrocyte sedimentation rate, GI = gastrointestinal, mRSS = modified Rodnan skin score, DAS-DU = Scleroderma Digital Ulcers Database, DUO = Digital Ulcers Outcome, DNSS = German Network for Systemic Sclerosis, CSRG = Canadian Scleroderma Research Group, EUSTAR = EULAR Scleroderma Trial and Research

SLE = systemic lupus erythematosus  PAH = pulmonary hypertension
Anisur Rahman (London, UK) brought the latest news about mechanisms of thrombosis in APS, based on the fact that the effects of antiphospholipids are not confined to thrombosis and that β2-glycoprotein 1 is a critical antigen. Other drugs besides anticoagulants may play a role in APS treatment, not only those that are already available (rivaroxaban, hydroxychloroquine, rituximab and complement inhibitors), but also new therapies such as DV inhibitors, DI variants, signaling inhibitors and TLR blockers.

George Bertias (Crete, Greece) stressed the need for therapeutic targets for SLE to be as available as for other chronic diseases, giving examples of possible candidates. One should prevent damage to ensure long-term survival and this can be accomplished by lowering disease activity, preventing flares by using hydroxychloroquine, avoiding long exposures to steroids, assessing comorbidities, and improving quality of life. On the other hand, clinically stable and inactive SLE should be managed with watchful waiting.

Finally, genetic factors in primary biliary cirrhosis were discussed by Pietro Invernizzi (Milan, Italy) who explained their importance in familial clustering, high concordance in monozygotic twins, sex chromosome defects (X-monosomy and Y-chromosome loss in males) and polymorphisms. In addition, the concept of a “second wave” represented by genome-wide association studies was highlighted because it has increased the genetic list, contrasting with the pre-GWAS era when only HLA-DRB1*08, HLA-DRB1*11 and HLA-DRB1*13 were known.

The next meeting on autoimmune diseases in Porto will be 12–14 February 2015.

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APS = antiphospholipid syndrome  
GWAS = genome-wide association studies

### Capsule

**Hearing sounds can improve your vision**

Sounds can draw our attention to a specific location and make us aware of something that we may otherwise overlook. But do auditory cues improve the function of other senses, such as sight? To find out, Feng et al. recorded the electrical activity in people’s brains when they were seeing and hearing stimuli. The researchers played a sound from one side and then quickly flashed a visual stimulus either on the same side or on the opposite side. When the sound and the visual stimulus came on the same side, electrical activity in the brain increased and people correctly identified the visual stimulus more often. This suggests that sound helps the brain process co-localized visual input.

*J Neurosci* 2014; 34: 9817
Eitan Israeli

### Capsule

**Tumorigenicity and genetic profiling of circulating tumor cells in small-cell lung cancer**

Small-cell lung cancer (SCLC), an aggressive neuroendocrine tumor with early dissemination and dismal prognosis, accounts for 15–20% of lung cancer cases and ~200,000 deaths each year. Most cases are inoperable, and biopsies to investigate SCLC biology are rarely obtainable. Circulating tumor cells (CTCs), which are prevalent in SCLC, present a readily accessible ‘liquid biopsy’. Hodgkinson et al. show that CTCs from patients with either chemosensitive or chemorefractory SCLC are tumorigenic in immune-compromised mice, and the resultant CTC-derived explants (CDXs) mirror the donor patient’s response to platinum and etoposide chemotherapy. Genomic analysis of isolated CTCs revealed considerable similarity to the corresponding CDX. Most marked differences were observed between CDXs from patients with different clinical outcomes. These data demonstrate that CTC molecular analysis via serial blood sampling could facilitate delivery of personalized medicine for SCLC. CDXs are readily passaged, and these unique mouse models provide tractable systems for therapy testing and understanding drug resistance mechanisms.

*Nature Med* 2014; 20: 897
Eitan Israeli

“**I have one share in corporate Earth, and I am nervous about the management**”

E.B. White (1899-1985), American writer and co-author of the English language style guide, *The Elements of Style*, commonly known as “Strunk & White.” He also wrote books for children, including *Charlotte’s Web*, *Stuart Little* and *The Trumpet of the Swan*