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Review

The 2014 ACR annual meeting: a bird's eye view of autoimmunity in 2015

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ABSTRACT

Our understanding of the mechanisms leading to rheumatic diseases is growing at unprecedented pace thanks to the worldwide network of clinical and translational researchers who gather at major scientific meetings to share their progresses. Further, these meetings allow the contamination of unrelated research areas and thus the spreading of ideas, hypotheses, and research tools. The annual meeting of the American College of Rheumatology (ACR) serves this purpose by allowing thousands of rheumatologists, immunologists, health care professionals, and basic scientists to attend the same sessions and present their work. The 2014 ACR meeting was held in Boston, MA, and was attended by over 16,000 participants who had the opportunity to directly witness the presentation of over 3000 abstracts. As such is the case, a full attendance of all update opportunities was not feasible. To fill this gap we arbitrarily selected the abstracts the appeared most interesting in a few fields of interest and we herein discuss the presented data and their further implications. In particular, we were intrigued by research advances in biomarkers for rheumatic diseases, and by advances on Sjögren syndrome, neuropsychiatric systemic lupus erythematosus, fibromyalgia, and B cell mechanisms. While we are well aware of the numerous blind spots that are expected in this type of article, we submit that this is far from a comprehensive overview and refer to the abstract book for a more complete analysis of the presented abstracts.

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1. Introduction

The November 2014 annual meeting of the American College of Rheumatology (ACR) took place in Boston, MA and included the presentation of 3018 abstracts either as oral lectures or posters over the four days of the scientific program. This year's ACR Meeting was host to nearly 16,000 participants in attendance from all over the world to learn and share the latest research discoveries as well as clinical guidelines and recommendations. While the abstract book is available freely online, the coauthors of this article have gathered their personal viewpoints on specific issues and arbitrarily selected a limited number of abstracts that appeared most interesting. We are well aware that the resulting report falls short of a proper summary of the meeting and cannot substitute the attendance but we are convinced that it may prove helpful both to attendees who had to choose other sessions as well as to colleagues who could not attend the meeting. We will discuss broad issues such as the proposed biomarkers for different conditions or B cell mechanisms as well as the proposed data from rheumatic diseases such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SjS), and fibromyalgia.

We apologize in advance for the numerous blind spots that to be expected in this type of article and would welcome any suggestion on future hot topics for a deeper analysis of the upcoming 2015 meeting in San Francisco, CA.

1.1. Biomarkers in connective tissue disease

Non-invasive biomarkers for rheumatic diseases remain an important field for investigation and the translation from the bench to the bedside is generally quite rapid, provided that confirmation is obtained in independent cohorts of patients. In particular, biomarkers are expected to provide advantages in three major ways. First, a reliable biomarker should allow an early diagnosis, particularly for diseases in which an early treatment is crucial to the prevention of progression and disability [1–4]. Second, it is important to identify patients who are likely to progress, thus allowing a correct allocation of therapeutic resources, especially for biologics [5–7]. Third, being able to predict the response to treatments would allow a more personalized treatment and again reduce the expenses for unjustified therapies [8–10].

In the field of idiopathic inflammatory myositis (IIM), including polymyositis and dermatomyositis, the number of associated serum autoantibodies continues to grow [11–13]. Mastka Kuwana and Colleagues [14] managed to detect dermatomyositis-specific auto-antibodies in 87% of 116 patients by adding immunoprecipitation (IP) assays combined with immunoblots to the commercially available MESACUP Anti-ARS test, while tested alone, MESACUP was positive in only 33% of the cases. Further, Siamak Moghadam-Kia and Colleagues [15], tested serum anti-MDA5 in a U.S. cohort of 122 dermatomyositis (DM) cases, of which 13% were positive and, more importantly, characterized by worse survival. As was previously reported in Asian population, this antibody was also found to be associated with interstitial lung disease (ILD) in this North American cohort. The differential diagnosis between IIM and statin-induced myositis may be challenging in clinical practice; further, while statin myotoxicity is generally self-limited, in some cases statin-exposed subjects may develop an autoimmune myopathy typically characterized by progressive weakness, muscle enzyme elevations, necrotizing myopathy on muscle biopsy and autoantibodies that recognize 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), the therapeutic target of statins. Patients with IIM have an increased risk of developing cardiovascular diseases and cardiovascular morbidity and mortality thus justifying a more accurate cardiovascular evaluation and possibly aggressive treatment of risk factors. Basharat and Colleagues evaluated the statin history, clinical features and prevalence of comorbidities in statin exposed patients with IIM according to the presence of HMGCR serum antibodies which were found in 77/1083 cases, with only 58 with previous statin exposure. Baseline features were similar between statin-exposed patients with and without HMGCR antibodies. The presence of HMGCR autoantibodies in statin-exposed patients was correlated with the activity of IIM, presented by a more prominent hip flexor weakness and higher mean creatine kinase plasma levels that required treatment with intravenous immunoglobulins and rituximab. The absence of anti-HMGCR antibodies was associated with a higher prevalence of distal weakness and interstitial lung disease. Statin-exposed anti-HMGCR-positive patients had an increased prevalence of cancer, although this difference was not statistically significant. Atorvastatin was used more frequently in HMGCR-positive patients who also had a higher prevalence of type 2 diabetes unrelated to steroids.

In the case of SLE, it is well established that serum autoantibodies, particularly anti-nuclear (ANA), appear decades before the clinical manifestations and diagnosis [16–18] and based on this observation Rufei Lu and Colleagues [19] analyzed 13 autoantibodies and 34 circulating soluble mediators in the sera of 55 patients with SLE defined by current classification criteria. Compared to healthy controls, elevated IL-4, IL-5 and IFN-γ levels were present in SLE sera long before formal disease classification ($\geq$3.4 years). Since IL-4 and IL-5 belong to the Th1 pathway and IFN-γ belongs to the Th2 pathway, this observation strengthens the hypothesis that both Th1 and Th2 pathways are involved in early SLE pathogenesis [16].

Malondialdehyde-acetaldehyde (MAA) derives from the lipid peroxidation of cellular membranes and binds to numerous macromolecules. Previous studies [20] have demonstrated that MAA-modified proteins elicit isotype-specific antibody responses and induce the expression of pro-inflammatory cytokines. Serum anti-MAA antibodies were found to be present in atherosclerosis, aortic aneurysm, alcoholic liver disease, and recently also in rheumatoid arthritis (RA) [21]. Andy Hollins and Colleagues reported that MAA IgG concentration are significantly higher in 88 SLE cases compared to controls while no difference was observed for MAA IgA concentration [22]. Whether MAA adduct formation and resulting immune responses mediate premature atherosclerosis in SLE is a fascinating hypothesis but certainly warrants further investigation [23,24]. Another abstract published by Thaschawee Arkachaisri and Colleagues from Singapore tested the diagnostic and prognostic roles of anti-C1q antibodies (aC1qAb) in 55 patients with childhood-onset SLE [25]. In agreement with previous studies in adult SLE, aC1qAb levels were found to be higher in patients with childhood-onset SLE compared with controls and aC1qAb levels were associated with the presence of nephritis and active disease compared to inactive disease.

Despite the presence of specific antibody against extractable nuclear antigens such as anti-Ro and anti-La, there is interest in the development of biomarkers for SjS [26–29], particularly for the risk of lymphoma [3,30] as will be discussed in a later paragraph. Mark Jasek and Colleagues tested the Sjö (R) diagnostic blood panel (including ANA, anti-Ro, anti-La, rheumatoid factor, and novel SjS autoantibodies including anti-salivary gland protein 1 -SP1-, anti-carbonic anhydrase 6 -CA6- and anti-parotid secretory protein -PSP-) [31,32] in 2306 patients with