This clinical form of OA may be associated with a so called "erosive" radiographic aspect marked by subchondral erosions of the finger joints and ankylosis. Many mediators of inflammation have been involved in the pathogenesis of osteoarthritis such as prostaglandin E2, free radicals and main cytokines (IL1B, IL6, and TNFa). Using Doppler power ultrasonography and magnetic resonance imaging, it has been shown that synovitis is frequently associated with HOA and correlates with pain and with disease progression.
Taking all those considerations together, it appears logical to target synovitis in HOA, especially with an erosive form.
Because erosive hand OA is a polyarticular disease, the treatment is more systemic than local.
Local or oral NSAIDS are out of scope because this presentation focuses on patients with HOA non responders to analgesics and NSAIDS. So far, none of the disease modifying drugs such as methotrexate has proved its efficacy.
Regarding biologics, several strategies have been approached. The first biotherapy used in HOA was IL2 receptor plus hydroxychloroquine in a very limited number of patients. Then and more recently, anti-TNFa strategy has been tested in well done RCT, in painful hand OA: one with adalimumab over a year, one with adalimumab 40 mg with 2 sub-cutaneous injections, one using Etanercept (50 mg/week 24 weeks and then 25 mg/week the next 24 weeks). None of those anti-TNFa blockers demonstrated a structural or an analgesic effect. However in the long term trial published by Verbruggen G, the incidence of new erosive lesions was decreased in Adalimumab group compared to placebo, only in a subgroup of patient with clinically inflamed IP joints.
Using anti-IL1B strategy, a decrease in pain has been observed in 3 patients using daily subcutaneous injection of Anakinra (100mg) over 3 months ( ).
In this Eular meeting a double inhibition of IL-1 Beta and IL-1 Alpha (using a monoclonal antibody directed against both cytokine) failed to demonstrate any benefit compared to placebo injection over 26 weeks.
Finally anti-IL6 strategy has been presented in this 2017 Eular meeting in a limited number of patients (n=18) with erosive HOA. Using monthly IV perfusion, the authors showed an improvement in pain level and functional status.
Conclusion: though anti-inflammatory strategy in painful HOA is logical, no treatment so far has been able to demonstrate a beneficial effect. Further studies should contemplate either news targets, or new modalities of repeated injections and should be adapted according to the phenotype of pain.
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Why we do develop autoimmunity

SP0181 FAILURE OF NATURAL REGULATORY AUTOANTIBODY NETWORK AS CAUSE OF AUTOIMUNITY

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The role of autoantibodies in normal physiology is under debate. In investigating autoantibody (aab) concentrations against G protein-coupled receptors (GPCR) in different autoimmune diseases, we found both increased and decreased aab concentrations, which suggests physiological anti-GPCR aab levels may be dysregulated in autoimmune diseases. During our analysis of healthy donor antibodies to 16 GPCR and 15 growth factors and related signaling molecules, we discovered several clusters of correlations in these antibody concentrations. Possible functional interactions of these 31 autoantibody target molecules were studied by STRING, DAVID, and enriched Gene Ontology analyses. Through these analyses, a network of GPCR, growth factors, and signaling molecules with endothelin receptor type A (ETAR) in the center was revealed. Migration and locomotion were suggested to be the most significant functions regulated by the antibody network. Accordingly, IgG from healthy donors induced both IL-8 expression by peripheral blood mononuclear cells (PBMCs) as well as migration of neutrophils and tumor cells, which was specifically diminished by the ETAR inhibition. These data supports a change of paradigm from the notion that autoantibodies are an exclusive autoimmune phenomenon to the concept that they are part of the normal human physiology, which become dysregulated under the influence of different factors and subsequently cause autoimmune diseases.
Disclosure of Interest: None declared
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SP0182 ALTERATIONS IN THE ANTIBODY REPERTOIRE AND SUGAR MODULATION AS CAUSE FOR AUTOIMMUNITY

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Many auto-immune diseases are hallmarked by the presence of auto-reactive B cells that can develop into autoantibody-secreting plasma cells. In most cases, the secreted autoantibodies have extensively been studied in their role as disease-associated biomarkers, and for some, specific pathogenic effector functions have been demonstrated supporting the use of interventions that target the plasma cell compartment. In other cases such as rheumatoid arthritis (RA), however, the pathogenicity of specific autoantibodies is less clear, and the therapeutic efficacy of B cell depleting therapy that spares the plasma cell compartment indicates that auto-reactive B cells themselves can have pathogenic effector functions that contribute to disease. In this context, it is of great interest to understand the mechanisms that allow auto-reactive B cells to emerge from the naïve repertoire, a process that marks the onset of systemic autoimmunity and frequently precedes the clinical onset of disease.
RA is characterized by a remarkable appearance of autoantibodies that target post-translational modifications of proteins, of which anti-citrullinated protein antibodies (ACPA) display the highest specificity for disease. In addition, ACPA associate with active destructive RA and pose individuals with arthralgia at-risk for progression towards arthritis. We recently found that ACPA display significant alterations with regard to the glycosylation of both the Fc-tail as well as the F(ab)-domain. While the ACPA-IgG Fc-tail loses galactose and sialic acid residues prior to the onset of arthritis, a process associated with enhanced inflammatory antibody activity that occurs potentially under the influence of IL-17 producing T cells, ACPA also carry abundant glycans in the antigen-binding region of the F(ab) domain. These latter glycans are reminiscent of F(ab)-glycans found in follicular lymphoma B cells, and were here identified as N-linked, biantennary glycans composed of a remarkably high frequency of sialic acid residues. Notably, N-glycosylation requires the presence of glycosylation consensus sequences in the protein. As such sequences are normally scarce in the germline encoded variable regions of B cell receptors (BCR), the acquisition of F(ab)-glycans requires mutations of the amino-acid sequence to generate N-glycosylation sites. This process is mediated by somatic hypermutation, which is mainly induced by T cells that provide help to B cells. As >90% of all ACPA-IgG molecules carry such F(ab)-linked N-glycans, and as protective antibodies in the same individuals and many autoantibodies in other diseases do not show this feature, it is conceivable that the acquisition of F(ab)-glycans by ACPA-IgG is a T cell –mediated process that provides a selective advantage to ACPA-expressing B cells. This notion is supported by the observation that additional F(ab)-glycans are not found on ACPA-IgM. How F(ab)-glycans facilitate the emergence and/or expansion of auto-reactive B cells in this context, however, remains unclear. Using recently developed technology to identify and isolate citrullinated antigen-specific B cells from patients, we can now address this question by studying the frequency and localisation of N-glycosylation sites in the antibody repertoire and by studying the phenotype and functional characteristics of ACPA-expressing B cells. Together with our investigations on the modulation of ACPA Fc-glycans, these studies provide a deeper understanding of mechanisms that allow the development of autoimmunity as such, and of the mechanisms that underlie the progression from systemic autoimmunity towards overt autoimmune disease.
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SP0183 FAILURE OF TREG CONTROL TO UNDERSTAND AUTOIMMUNITY

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Regulatory T cells (Treg) expressing the transcription factor FoxP3 are crucial for the maintenance of immunological tolerance to self and thus for the control of autoimmunity. There is strong evidence that numeric or functional defects in Treg cell biology are involved in the pathogenesis of particular autoimmune diseases. Here we will focus on the fundamental role of Treg cells in diverse autoimmune and rheumatic diseases and will explain how a failure of the Treg cell system can evolve and contribute to the development of such diseases. Furthermore, therapeutic approaches aiming to overcome these Treg cell defects and to restore Treg cell activity in the patients will be discussed.
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SP0184 ROLE OF MICROENVIRONMENT AND ENDOGENOUS PATHWAYS TO BREAK TOLERANCE

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Break of tolerance driving autoimmune disease is initiated by a combination of predisposing genetic and environmental factors resulting in self-perpetuating chronic inflammation and tissue damage. Effector molecules and cells targeting tissues housing the inciting autoantigen(s) maintain tissue damage and the autoimmune response. Granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis) is a prototypical autoimmune disease characterized by extravascular necrotizing granulomatous inflammation and a systemic autoimmune vasculitis associated with anti-neutrophil cytoplasmic autoantibodies specific for the neutrophil- and monocyte-derived serine-protease proteinase 3 (PR3-ANCA). GPA is strongly associated with *HLA-DPB1*0401* polymorphisms. Its association with the *R620W* variant of the *PTPN22* gene has been linked to reduced immune-regulatory interleukin (IL)-10 transcription. Epidemiological studies and molecular analysis of immune cells suggests a multifactorial pathogenesis of GPA, in which a potentially metachronous and individually varying sequence of infectious agents contributes to the break of tolerance and chronic inflammation sustaining autoimmunity in GPA.