

Objectives: The purpose of the effort was to increase patient safety and to ensure that patients received independent patient information within biological drugs.

Methods: First the Association conducted a small study of how the shift of drug had taken place in the different regions. Most patients experienced that they were told by the doctors to shift to biosimilars, and furthermore they experienced a lack of information about the new biosimilars. On a national level, nearly all patients on a biological drug are registered in a national database. It is registered in the database and hospital records which drug the patient are prescribed, but it is not registered on a batch-level.

In order to change these conditions the Association started a dialog with the politicians and the authorities on a national level and the hospital-administrations on a regional level. The purpose was to improve the registration of the drugs on batch-level, to improve more independent patient information and to improve the involvement of the patient in the decision making process. The dialog was on a general level, but with several patient-stories from each region.

Results: A new national plan for better monitoring and information about biologic and biosimilars was launched in august 2015 and carried out in 2016. The plan consists of four parts: 1) Monitoring biological drugs and biosimilars on batch level, 2) Information campaign to health professionals and patients, 3) Digital solutions and easy reporting of side effects from health professionals and patients, 4) Focus on monitoring patient safety by the authorities. The Danish Rheumatism Association has participated in the work to implement the plan. In addition to the national plan the hospitals on a regional level, has invited the Rheumatism Association to participate with a representative in the working group, where national recommendations for the use of biological drugs are being made in an attempt to involve the patient perspective more. The content of the national plan and the involvement in the work with national recommendations, will be elaborated and discussed from the patients perspective throughout the presentation.

Conclusions: The implementation of biosimilars created great insecurity among patients. Therefore, the Danish Rheumatism Ass. decided to make an effort to create better patient information and safety for the patients. Through dialog with politicians, national authorities and hospital-administrations, we managed to get a national plan for better monitoring and information about biologic and biosimilars, and to be involved in the work with national recommendations for these drugs. The national plan and work with national recommendations will be elaborated in the presentation.

Disclosure of Interest: None declared

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Switching T on and off: how T cells drive and regulate chronic inflammation

OP0329 INVOLVEMENT OF T HELPER 17 CELLS IN INFLAMMATORY ARTHRITIS DEPENDS ON THE HOST INTESTINAL MICROBIOTA

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Background: Intestinal microbiota have been associated with psoriatic and rheumatoid arthritis. One of the major effects of microbiota is the induction of mucosal T helper 17 (Th17) cells. We therefore reasoned that the efficacy of Th17-targeted therapies in arthritis may depend on the host microbiota. Previous studies focused on the role of the cytokine interleukin-17A (IL-17), rather than Th17 cells, by using IL-17 inhibitors or IL-17-deficient mice. Therefore, the role of Th17 cells, which produce multiple pro-inflammatory mediators in addition to IL-17, is not yet fully understood.

Objectives: The aim of this study was to determine the role of Th17 cells, beyond the cytokine IL-17, in arthritis, and to investigate whether Th17 cells are differentially involved in arthritis depending on the microbiota present.

Methods: We established conditional Th17-deficient mice, which exhibit a CD4-Cre-induced floxing of a part of the Rorc allele that encodes the Th17 master regulator ROR γ t. We compared the development of collagen-induced arthritis in Th17-deficient (CD4-Cre⁺ Rorc^{flox/flox}) and -sufficient (CD4-Cre⁺ Rorc^{flox/flox}) littermate mice, either colonized with known Th17 cell inducers segmented filamentous bacteria (SFB) or harboring the SFB-free Jackson microbiota. The abundance of Th1 and Th17 cells and the production of IL-17, IFN γ and GM-CSF were quantified by flow cytometry and multiplex cytokine assay.

Results: CD4-Cre⁺ Rorc^{flox/flox} mice had significantly lower Th17, but similar Th1 cell abundance, in intestinal lamina propria compared with Cre⁺ littermate controls. Surprisingly, the total amount of IL-17A production by all lamina propria cells during arthritis was rather increased in Th17-deficient mice, with CD8⁺ T cells and Gr1⁺ neutrophils being the main alternative sources of IL-17. Despite this increased total IL-17 levels, conditional Th17-deficient mice developed a less severe arthritis compared with Th17-sufficient mice when intestinal microbiota comprised SFB. This suggests a role for Th17 cells in inflammatory arthritis distinct from IL-17. Accordingly, synovial inflammation, cartilage destruction and

proteoglycan depletion were reduced in SFB-colonized Th17-deficient mice. While the production of IL-17 by joint-draining lymph node cells stimulated with PMA and ionomycin was similar between Th17-sufficient and -deficient mice, cells from the latter group produced significantly less IL-17 upon antigen-specific stimulation with type II collagen. Furthermore, the production of GM-CSF, another Th17 cell-derived cytokine, was significantly lower in the lymph nodes of Th17-deficient mice, an effect associated with the protection against arthritis. Importantly, substitution of the intestinal microbiota with SFB-free Jackson microbiota resulted in the loss of Th17 cell dependency of arthritis as Th17-sufficient and -deficient mice showed similar disease progression under this condition.

Conclusions: These data suggest that Th17 cells may mediate inflammatory arthritis partly through IL-17-independent mechanisms. Our observations also suggest that the involvement of Th17 cells in arthritis depends on the microbiota subset present in the host. Therefore, a microbiome-guided stratification of rheumatoid or psoriatic arthritis patients might improve the efficacy of Th17 (or IL-17)-targeted therapies.

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OP0330 FRA2 OVEREXPRESSION LEADS TO SYSTEMIC AUTOIMMUNITY BY DECREASING IL-2 RESPONSIVENESS AND THYMIC TREG DEVELOPMENT

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Background: Fos-related antigen 2 (Fra2) is a transcription factor belonging to the Fos family proteins which is part of the AP-1 transcription complex. We recently described a Fra2 transgenic (tg) mouse model which develops a multi-organ inflammatory phenotype affecting skin, lungs, thymus, liver and salivary glands. We have observed abnormalities in the T cell compartment, particularly in regulatory T (Treg) cells, which led us to hypothesize that Fra2 tg mice develop a T cell driven autoimmune phenotype.

Objectives: To demonstrate the autoimmune phenotype of Fra2 tg mice and to characterize the mechanisms leading to Treg cell abnormality.

Methods: We used previously generated Fra2 tg overexpressing mice. T lymphocyte populations were analyzed by flow cytometry for expression of activation markers and secretion of cytokines. We transferred purified CD4⁺ T cells into Rag2^{-/-} mice lacking T and B cells, and we generated Rag2^{-/-}/Fra2 tg mice. Bone marrow cells were transferred into lethally irradiated recipients to create Fra2-WT bone marrow chimeric mice.

Results: Fra2 tg mice backcrossed onto a Rag2^{-/-} background did not develop inflammatory manifestations (n=6), demonstrating the dependence on T and/or B cells of the autoimmune phenotype. In line with this, the transfer of purified CD4⁺ cells from 16 week-old Fra2 tg mice into Rag2^{-/-} recipients was sufficient to transfer the disease phenotype (n=3). Analysis of T cell populations from Fra2 tg mice showed the presence of activated CD4⁺ and CD8⁺ cells in the spleen

Graphical abstract

