who have developed RA so far and patients with arthralgia or at the time of RA manifestation.

**Conclusion:** We identified lower number of NK cells as well as NK-T and γδ-T cells in individuals at risk of developing of RA. The decrease in non-conventional T cells was observed despite the increased percentage of the classical T cells. We hypothesize that the disproportionate of these lymphocyte subpopulations, described previously in established RA, observed here in at-risk individuals may reflect their predisposition for further development of RA.

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**THU0084 TOFACITINIB REVERSED ENDOTHELIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS: MECHANISTIC INSIGHTS FROM THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL.**

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**Background:** Tofacitinib, an inhibitor of JAK3 and JAK1, is approved for the treatment of rheumatoid arthritis (RA)1. Cardiovascular (CV) risk2 and events3 in RA patients treated with Tofacitinib is a matter of debate, but the vascular mechanisms involved are unknown.

**Objectives:** The aim of this study was to investigate whether Tofacitinib improves endothelial dysfunction (ED) and if so to explore the underlying mechanisms in the model of adjuvant-induced arthritis (AIA) in rats.

**Methods:** AIA was induced by injection of Mycobacterium butyricum in the tail of male Lewis rats. A group of rats without arthritis served as controls. At the first signs of arthritis, AIA-received Tofacitinib (10mg/kg twice daily, s.c.) or 33%DMSO/PEG (Vehicle). Arthritis score was daily evaluated. After 21 days, preconstricted isolated aortic rings were relaxed with acetylcholine (SNP, 10⁻¹⁰⁻¹⁻¹⁻¹⁻¹ moles/liter). Blood pressure and heart rate were measured by invasive method. A radiographic score was attributed to hind paw.

**Results:** Compared to AIA-Vehicle, Tofacitinib dramatically reduced arthritis (-76%) and radiographic (-73%) scores (p<0.001), and improved Ach-induced vasorelaxation (p<0.05). Of note, Ach-induced vasorelaxation was not different between Tofacitinib-AIA and control rats. The response to SNP was not different between groups. The effect of Tofacitinib on ED was mediated by decreased cyclooxygenase-2 and arginase activities, decreased superoxide anions production, increased NO synthase activity and EDHF synthesis. As compared to AIA-Vehicle, Tofacitinib changed neither blood pressure nor heart rate.

**Conclusion:** The present results demonstrated that Tofacitinib reversed arthritis-induced ED, through the correction of all the acknowledged impaired endothelial pathways in the AIA model. As ED is the primus mover of atherogenesis, these data provide a mechanistic explanation to the potential benefits of Tofacitinib on the cardiovascular comorbidities associated to RA.

**References:**


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**THU0085 RESOLVIN D5 MODULATES TH17/TREG CELL DIFFERENTIATION AND SUPPRESSES OSTEOCLASTOGENESIS**

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**Background:** Resolution phase of acute inflammation has been recognized not passive but active process during the last 2 decades. This active process is highly regulated by novel families of potent bioactive lipid mediators, which are coined as specialized proresolving mediators (SPMs) including resolvins. Little has been known, however, about how resolvins are involved in chronic inflammation, such as rheumatoid arthritis (RA).

**Objectives:** To investigate whether lipid mediators (LM) are involved in the pathogenesis of RA.

**Methods:** We investigated lipid mediator profiling in the paws of SKG arthritis mice by using lipid chromatography (LC) mass spectrometry (MS) /MS-based LM metabololipidomics. CD4⁺ T cells from spleens of SKG mice were cultured on anti-CD3/CD28Abs precoated plate with IL-6/TGF-β, anti-IFNγ/IL-4 and analyzed by flow cytometry. CD4⁺ T cells were labeled with CFSE, and cell proliferation was analyzed by flow cytometry. Mouse bone marrow cells were cultured with M-CSF and RANKL, and TRAP-positive multinucleated cells were defined as osteoclasts. Osteoclast differentiation markers were analyzed by qRT-PCR.

**Results:** RvD5 or normal saline was administered daily into the peritoneal cavity of arthritic SKG mice. Among the elevated SPMs, only RvD5 was detected in RvD5-treated mice than that in control group, although there was no significant difference. In Patients With Rheumatoid Arthritis. Arthritis Rheumatol. (2019);71(9):1450-1459.

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**Figure 1**