Introduction Macroautophagy is an important contributor of cellular homeostasis, and therefore is active and up regulated in various conditions of cellular stress and inflammation. The pathway has been implicated in shaping the innate and adaptive immune responses by acting at multiple and diverse levels including cytokine secretion and antigen presentation.

Objectives Our aim is to analyse the contribution of macroautophagy in antigen presenting cells to the adaptive immune response in the context of arthritis. We analysed the antigen induced arthritis model in mice that are deficient in autophagy in their dendritic cells.

Methods CD11c-Cre mice (C57BL/6), (Jackson Laboratory) were crossed with Atg5lox/lox mice (C57BL/6) provided by Dr. Noboru Mizushima (Japan). ATG5 is an essential autophagy gene, its targeted deletion in dendritic cells completely abolished a functional autophagy pathway in these cells (DC/ATG5-/-). For the antigen induced arthritis mice model (AIA), mice were immunised with methylated BSA (mBSA) and CFA. Monoarthritis was induced at day 21 by injection of mBSA into the knee joint and animals sacrificed at day 28. Sections from knees were stained with haematoxylin and eosin for macroscopic scoring of the cellular infiltrate. In parallel, toluidine blue staining was used for cartilage damage. T cell function was monitored by cytokine production by ELISA, after in vitro re-stimulation with mBSA or CD3/CD28 for 72 hour, using single cell suspensions from lymph nodes.

Results Mice lacking autophagy in their dendritic cells (DC/ATG5-/-) showed enhanced cartilage destruction and bone erosion. Interestingly, the Th1/Th17 response in DC/ATG5-/- mice was significantly increased. In parallel this phenotype was linked to a decreased Foxp3 expression in the regulatory T cell (Treg) population. Using Treg transfer upon AIA we could demonstrate that regulatory T cells switch to Th17 cells in the context of inflammation.

Conclusions Autophagy deficiency in dendritic cells exacerbates the Th1/Th17 inflammatory response in the AIA model, resulting in increased cartilage destruction and bone erosion. This phenotype is linked to Tregs instability upon inflammation.

Disclosure of interest None declared