neutrophel elastase (NE), proteinase 3 (PR3), and cathepsin G (CG) and myeloperoxidase (MPO) expression by qRT-PCR. NE/PR3/CG triple knockout mice and in vitro depletion of neutrophils approaches were performed to determine the role of NSPs and neutrophils in estrogen-mediated inflammatory responses. The splenic neutrophil and NSPs expression in lupus-prone MRL-lpr, B6-lpr and NZB/W_F1 and their respective controls were also analysed.

Results Although oestrogen reduced total splenocytes number, it markedly increased the splenic neutrophil numbers, NSPs and MPO expression in B6 mice (Figure 1). Splenic neutrophils, NSPs and MPO were also significantly increased in MRL-lpr, B6-lpr and NZB/W_F1 mice (Figure 2). Despite of the critical role of NSPs and neutrophils in inflammation, depletion of NSPs in vivo did not affect oestrogen’s ability to increase in splenic neutrophils nor the induction of inflammatory mediators from ex vivo activated splenocytes, and depletion of splenic neutrophils in vitro had also no obvious effect on NSPs expression (due to the increase of NSPs in cells other than neutrophils) and LPS-induced IFNg and MCP-1 (Figure 3).

Conclusions Overall, we demonstrated a remarkable commonality with regards to the increase of neutrophils and NSPs in the spleens of autoimmune-prone mice and estrogen-treated B6 mice.

114 N-ACETYL-L-CYSTEINE (NAC) CONTROLS OSTEOCLASTOGENESIS THROUGH REGULATING TH17 DIFFERENTIATION AND RANKL PRODUCTION IN RHEUMATOID ARTHRITIS
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Background and aims This study aimed to determine the regulatory role of N-Acetyl-l-cysteine (NAC), an antioxidant, in IL-17-induced osteoclast differentiation in rheumatoid arthritis (RA).

Methods After RA synovial fibroblasts were stimulated by IL-17, the expression and production of RANKL was determined by real-time PCR and ELISA. Human peripheral blood monocytes were cultured with M-CSF, IL-17, RANKL, and/or various concentrations of NAC, followed by counting of the cells for tartrate-resistant acid phosphatase activity to determine osteoclast formation. Osteoclastogenesis was also determined after cocultures of IL-17-stimulated RA synovial fibroblasts, Th17 cells and various concentrations of NAC with monocytes. After human peripheral CD4+T cells were cultured with NAC under Th17 condition, IL-17, IFN-g, IL-4, Foxp3, RANKL and IL-2 expression and production was determined by flow cytometry or ELISA.

Results When RA synovial fibroblasts were stimulated by IL-17, IL-17 stimulated the production of RANKL, and NAC reduced the IL-17-induced RANKL production in a dose-dependent manner. NAC decreased IL-17-activated phosphorylation of mTOR, JNK and IκB. When human peripheral blood CD14+ monocytes were cultured with M-CSF and IL-17 or RANKL, osteoclasts were differentiated, and NAC reduced the osteoclastogenesis. After human peripheral CD4+ T cells were co-cultured with IL-17-pretreated RA synovial fibroblasts or Th17 cells, NAC reduced their osteoclastogenesis. Under Th17 polarising condition, NAC decreased Th17 cell differentiation and IL-17 and RANKL production.

Conclusions NAC inhibits the IL-17-induced RANKL production in RA synovial fibroblasts and IL-17-induced osteoclast differentiation. NAC also reduced Th17 polarisation. NAC could be a supplementary therapeutic option for inflammatory and bony destructive processes in RA.