most abundant leukocytes in Human blood, but it is not clear whether neutrophils exert an important role in the pathogenesis of organ tissue damage in SLE.

**Methods** We used lupus-prone mouse model and model of lupus serum-induced tissue inflammation in mouse to investigate the role of neutrophils in the organ damage of SLE.

**Results** We found that there was a little neutrophil infiltration in the inflammatory sites of skin, liver, brain and joint in lupus-prone mice. We also found that there was also little neutrophil infiltration in the site of skin inflammation induced by lupus serum in normal mouse. The severity of skin inflammation induced by lupus serum was not significantly decreased in mice with neutrophil depletion compared to ones without neutrophil depletion. But we found that neutrophils were actually involved in tissue injury induced by lupus IgG. Further studies showed that lupus IgG stimulated and activated neutrophils, and cause the death of neutrophils. Studies also confirmed that Fas plays an important role in neutrophils apoptosis.

**Conclusions** Our study indicates that neutrophils participate in the early stage of lupus organ damage, and then they died through activation-mediated apoptosis. These findings promote the understanding of the role of neutrophils in the tissue injury with SLE.

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**TLR8 ACTIVATION IN NEUTROPHILS IMPAIRS IMMUNE COMPLEX PHAGOCYTOSIS THROUGH FURIN-DEPENDENT SHEDDING OF FCGRIIA**

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**Background and aims** Neutrophils play a crucial role in host defense through mechanisms including phagocytosis and formation of neutrophil extracellular traps (NETs), a recently identified neutrophil cell death process in which DNA is extruded together with cytoplasmic and granular content to trap and eliminate extracellular pathogens. Although beneficial from a host-pathogen perspective, exaggerated neutrophil activation has been linked to autoimmunity, in particular the rheumatic disease systemic lupus erythematosus (SLE) where nucleic acid-containing immune complexes (IC) drive inflammation. Toll-like receptor (TLR) agonists, such as nucleic acid-containing immune complexes (IC) drive inflammation. Toll-like receptor (TLR) agonists, such as nucleic acids, are important components of pathogens, enabling phagocytosis by macrophages and dendritic cells, but the role of TLR signalling in processing of SLE ICs and downstream inflammatory neutrophil effector functions is not known.

**Methods** Standard Methods.

**Results** We observed that both FcgR- and TLR8-engagement were required for induction of NETosis, whereas TLR8 activation, through the RNA component of the ICs, suppressed further IC-mediated phagocytosis. Mechanistically, TLR8 ligation-induced PI3K-dependent ROS generation through NADPH oxidase, and subsequent furin-dependent proteolytic cleavage of the N-terminal part of FcgrIIA shifting neutrophils away from phagocytosis of ICs toward NETosis. TLR8 activated neutrophils promoted cleavage of FcgRIIA also on plasmacytoid dendritic cells and monocytes resulting in impaired overall clearance of ICs and increased complement C5a generation. Importantly, ex vivo derived activated neutrophils from SLE patients demonstrated a similar cleavage of FcgRIIA that was correlated with markers of disease activity as well as complement activation.

**Conclusions** Therapeutic approaches aimed at blocking TLR8 activation would be predicted to increase phagocytosis of circulating ICs while disarming their inflammatory potential.