**Introduction and Aims:**
Using DNA and microRNA arrays, we have previously shown that patients with active Systemic Lupus Erythematosus (SLE) express a strong neutrophil and autophagy signature. We have also shown that tissue factor (TF), an in vivo initiator of the coagulation cascade and a trigger of inflammation, is released on Neutrophil Extracellular Traps (NETs). Herein, we sought to investigate the role of TF-decorated NETs in SLE and their involvement in lupus nephritis.

**Methods:**
Serum and neutrophils from 15 healthy donors and 20 SLE patients (15 active, 5 on treatment with hydroxychloroquine) were isolated. Cultures of ex vivo neutrophils or in vitro stimulation and inhibition studies were performed. Autophagy levels were evaluated by confocal microscopy and immunoblotting. NET release was studied by confocal microscopy, and NETs were measured with MPO/DNA complex ELISA. TF expression and activity were studied by confocal microscopy and TAT-complex ELISA, respectively. Kidney biopsies from 5 patients with lupus nephritis were analyzed for the presence of TF-decorated NETs.

**Results:**
Neutrophils from active SLE patients express increased autophagy levels and undergo increased NETosis in an autophagy-mediated manner. NETs released from active SLE patients are decorated with active TF and lead to thrombin generation and PAR-signaling activation. Furthermore, serum from active SLE patients induces autophagy-dependent NET release and TF up-regulation in healthy neutrophils, suggesting that the inflammatory environment of SLE mediates these processes. In line with these, treatment of patients with hydroxychloroquine, an autophagy inhibitor, reverses the observed phenomena. Importantly, TF-decorated NETs are present in the kidneys of patients with lupus nephritis even in the absence of neutrophils within the tissue.

**Conclusions:**
Neutrophils from active SLE patients display increased autophagy and also undergo increased NETosis in an autophagy-mediated manner that is inhibited by hydroxychloroquine. TF-enriched NETs within the kidney may mediate renal injury in the absence of neutrophils. Autophagy-dependent delivery of TF on NETs provides a link between increased thrombogenicity and inflammation observed in SLE, and may explain the salutary effects of hydroxychloroquine in lupus nephritis. Our findings propose a novel mechanism of renal injury in lupus nephritis.