

17 ENHANCED RELEASE OF NEUTROPHIL EXTRACELLULAR TRAPS FROM PERIPHERAL BLOOD NEUTROPHILS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background/objectives Neutrophils are the most abundant cell type identified in joints from patients with rheumatoid arthritis (RA), with a key role in inflammation and cartilage damage. Activated neutrophils may form extracellular traps (NETs), with potent pro-inflammatory and immunostimulatory activity. The authors sought to assess the role of NET release in RA pathogenesis.

Materials/methods Peripheral blood neutrophils from RA patients (n=3) (DAS28>5.1) and control subjects (n=7) were isolated. NET formation from RA neutrophils and control neutrophils treated with RA serum (n=7) or synovial fluid (n=2) was assessed by immunofluorescence microscopy, using co-staining with myeloperoxidase and DAPI. The percentage of NET releasing cells was determined by examining 200 cells per sample in a double blind fashion. Time course experiments revealed optimal NET release at 3 h.

Results Freshly isolated RA neutrophils underwent spontaneous NET release at higher rates compared to normal controls (11.67±2.1% vs 3.21±0.9%, p<0.05). Treatment of control neutrophils with RA serum increased NET release compared to cells treated with normal serum (16±2.5%, p<0.005). Increased NET formation (approximately 3-fold induction) was observed in control neutrophils incubated with RA synovial fluid. Inhibition studies in progress address the impact of inflammatory cytokines and/or immune complexes in NET production as well as the impact of NETs on dendritic and T cell activation.

Conclusions Neutrophil activation in RA is associated with enhanced NET formation, driven by soluble factors found in RA sera and synovial fluid. Whether NETs are involved in the cross-talk between neutrophils and adaptive immune responses in RA is under investigation.