# The role of extracellular DNA in pathogenesis of rheumatoid arthritis

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease. The exact etiopathogenesis of RA is not yet known. Extracellular DNA (ecDNA) appears to be one of key players in pathogenesis based on its inflammatory properties. One of the sources of ecDNA is the activity of neutrophils mostly production of neutrophil's extracellular trap (NETs), where ecDNA is mayor component.

**Methods:** In confirmed RA patients, blood collection was realized before initiating treatment with bDMARDs and at 3 and 6 months post-treatment. Clinical parameters such as C-reactive protein (CRP) and disease activity score (DAS28) were utilized. Analysis of ecDNA was performed from blood samples. In the collagen-induced arthritis (CIA) model and collagen-antibody-induced model the effects of DNase I and NETs inhibitor were studied. Arthritic score was assessed, together with the main signs of inflammation.

**Results:** In clinical samples ecDNA significantly decreased by 31% ($p=0.02$) from the baseline, before the bDMARDs, to 6 months after the treatment, meanwhile by DAS28 and CRP decreased by 51% and 76% respectively. The animal model showed a nearly threefold difference in ecDNA concentration between untreated CIA mice and those treated with DNase I ($p=0.03$). In the treated CIA group, serum DNase activity was almost five times higher than in the untreated CIA females. Mice receiving NETs inhibitor showed a lower points of arthritis score than arthritic group of mice (0 vs. 6 points, $p<0.05$).

**Conclusion:** To conclude, ecDNA may play a significant role in the pathogenesis of RA. The association between ecDNA and the importance of neutrophils in RA etiology has been highlighted by our results showing reduced symptom severity and delayed onset of symptoms following the application of NETs inhibitors. These results suggest that NETs compartments, mainly ecDNA could serve as a component of rheumatoid arthritis and potentially become early predictive markers.