26 LL-37 IS EXPRESSED IN THE INFLAMED SYNOVIUM IN PATIENTS WITH RHEUMATOID ARTHRITIS AND DOWNREGULATED BY TNF INHIBITORS

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Background/objectives LL-37, a member of the cathelicidin family of host defense peptides, has a broad range of immunomodulatory and anti-infective effects that are known to selectively alter innate immunity. The authors aimed to investigate a potential role of LL-37 in rheumatoid arthritis (RA).

Materials and methods Thirty-eight patients meeting the 1987 American College of Rheumatology (ACR) criteria for RA were recruited for this study. The authors evaluated LL-37 and CD-68 expression by immunohistochemistry in synovial biopsy samples obtained before and after a mean of 8 weeks of treatment from 15 patients treated with adalimumab, 12 patients treated with etanercept and 11 patients treated with Methotrexate. The authors also evaluated LL-37 expression in 10 healthy controls. Microscopic analysis was performed and stained synovial biopsy sections were evaluated semiquantitatively in random order by two independent observers (ME and PN) using a four-point scale (0=no positive cells, 1=occasional positive cells, 2=scattered positive cells and/or focal positive cells, 3=extensive positive cells). The observers were unaware of patient identity. Statistical analysis was performed using Wilcoxon paired test.

Results LL-37 was expressed in most of the RA synovial biopsies, both in close proximity to blood vessels and in the lining and sublining layers. Serial immunostaining for cell surface markers identifies macrophages and granulocytes as main cells expressing LL-37 in the inflamed joint. Lower expression of LL-37 was observed in the healthy controls. Interestingly the authors were able to demonstrate a significant downregulation of LL-37 following adalimumab and etanercept but not methotrexate treatment.

Conclusion Our results suggest a role for LL-37 in the synovial inflammation and show specific regulation of this molecule by distinct antirheumatic agents.