Nature Reviews Rheumatology **10**, 446 (2014); published online 8 July 2014; doi:10.1038/nrrheum.2014.112

RHEUMATOID ARTHRITIS

Citrullination alters the inflammatory properties of chemokines in inflammatory arthritis

Chemokine citrullination in inflamed joints, and the resultant monocyte recruitment, could accelerate disease progression in rheumatoid arthritis (RA), according to a study by Yoshida *et al.* published in *Arthritis & Rheumatology.*

> “Joints injected with citrullinated CXCL5 became more inflamed and recruited more monocytes...”

Chemokines are involved in recruiting monocytes and polymorphonuclear cells (PMNs) to sites of inflammation, such as the joints in early RA. Citrullination of chemokines can regulate their inflammatory properties, but whether this post-translational modification is relevant to the role of chemokines in the initiation of inflammatory arthritis was, until now, unknown.

First, Yoshida and colleagues showed that citrullinated chemokines are found in the synovial fluid of patients with RA and that they are present at higher levels than in healthy controls or patients with other rheumatic diseases. Next, they asked whether the levels of these chemokines correlate with disease activity: levels of citrullinated CXC-chemokine ligand (CXCL) 5 (also known as epithelial-derived neutrophil-activating peptide 78; ENA-78), but not noncitrullinated CXCL5 or the other chemokines studied, directly correlated with C-reactive protein levels and erythrocyte sedimentation rates in these patients.

These findings suggest a role for citrullinated CXCL5 in the pathogenesis of inflammatory arthritis, but which cells does this chemokine influence? Through performing *in vitro* chemotaxis assays, the researchers found that citrullination of CXCL5 increased the monocyte-migratory capacity of this chemokine but reduced its ability to recruit PMNs.

To confirm if this increased monocyte recruitment also occured *in vivo,* Yoshida *et al.* injected noncitrullinated or citrullinated CXCL5 into the knee joints of mice and measured joint inflammation and monocyte migration. Joints injected with citrullinated CXCL5 became more inflamed and recruited more monocytes than those injected with noncitrullinated CXCL5.

The authors conclude that citrullination of CXCL5 changes its inflammatory properties and leads to an increased monocyte-recruiting capacity for this chemokine and a role in RA pathogenesis.

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Original article Yoshida, K. *et al.* Citrullination of ENA-78/CXCL5 results in conversion from a non-monocyte recruiting to a monocyte recruiting chemokine. *Arthritis Rheum.* doi:10.1002/art.38750