

SPONDYLOARTHROPATHIES

MIF drives inflammation and bone formation in AS

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Inflammation and new bone formation are hallmarks of disease progression in ankylosing spondylitis (AS). A new study published in *Arthritis & Rheumatology* now shows that macrophage migration inhibitory factor (MIF) not only promotes inflammation, but also triggers osteoblastic activity, suggesting a novel pathogenic role for this pleiotropic cytokine in AS.

The study's corresponding author Nigil Haroon explains that his group's interest in this area started with reports of antibodies against CD74 being detected in patients with spondyloarthritis. Given that CD74 is the cognate receptor of a potent pro-inflammatory cytokine (MIF), and that MIF reportedly also had effects on bone, their current work tested the hypothesis that the MIF–CD74 axis

could represent a link between inflammation and new bone formation in AS. “We have shown that MIF can drive both processes effectively and its effects seem to be mediated through its receptor CD74,” explains Haroon.

The investigators first demonstrated that serum levels of MIF were raised in patients with AS as compared with healthy individuals. Moreover, serum MIF levels were higher in patients with AS who were defined as ‘progressors’ (that is, those with a rate of increase in their modified Stoke AS spine score (mASSS) of ≥ 1 unit per year) than in ‘non-progressors’, and both serum MIF level and baseline mASSS independently predicted radiographic progression.

Tissue analyses revealed increased levels of MIF in the synovial fluid and high frequencies of MIF-producing

macrophages and Paneth cells in the ileum of patients with AS.

In vitro, MIF induced monocyte-specific TNF production and enhanced mineralization and osteoblastic gene expression in osteoblast cell lines. MIF signalling was found to act via activation of β -catenin.

The researchers plan to explore MIF as a biomarker for AS diagnosis and prognostication. “We are also exploring therapeutically targeting MIF in AS,” says Haroon.

Sarah Onuora

ORIGINAL ARTICLE Ranganathan, V. et al. Macrophage migration inhibitory factor induces inflammation and predicts spinal progression in ankylosing spondylitis. *Arthritis Rheumatol.* <http://dx.doi.org/10.1002/art.40175> (2017)

FURTHER READING Ranganathan, V. et al. Pathogenesis of ankylosing spondylitis — recent advances and future directions. *Nat. Rev. Rheumatol.* 13, 359–367 (2017)