Nature Reviews Rheumatology | Published online 1 Jun 2017; doi:10.1038/nrrheum.2017.89

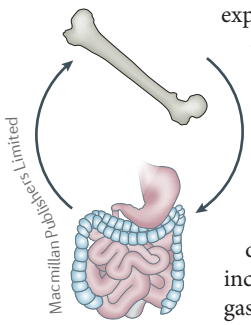
SPONDYLOARTHROPATHIES

Gut–bone crosstalk in HLA-B27 rats

> Treatment with broad-spectrum antibiotics … reduced the number of CD43^{lo} monocytes

HLA-B27, a known genetic risk factor for ankylosing spondylitis, is associated with spondyloarthritis-like symptoms in HLA-B27 transgenic rats that begin in the gut and spread to the joints. New research is beginning to unravel the links between gut inflammation and arthritis in this model of ankylosing spondylitis, with the microbiota thought to be pivotal in controlling disease progression.

"It is now appreciated that dysbiosis and gastrointestinal inflammation are key components of HLA-B27^{+} spondyloarthropathies, but we still do not understand how the various factors initiate or contribute towards the multisystemic inflammatory-driven pathology," explains Carl Goodyear, corresponding author on the new study. "Human HLA-B27 transgenic rats display a plethora of the pathological aspects of the spondyloarthropathies, including dysbiosis, gastrointestinal inflammation and skeletal changes. They represent an excellent model for investigating the interaction and/or contribution of the various biological systems," he continues.



Previous studies revealed that germ-free HLA-B27 transgenic rats do not develop gut or joint pathologies, indicating a clear association between the gut microbiota and pathogenesis. Taking this concept forward, Goodyear and colleagues found that reducing gut inflammation in HLA-B27 transgenic rats by treating them with broad-spectrum antibiotics affected circulating levels of pro-inflammatory cytokines, chemokines and osteoclast precursor cells.

HLA-B27 transgenic rats had increased numbers of CD43^{lo} conventional monocytes in their blood and bone marrow compared with wildtype and HLA-B7 transgenic rats. These CD43^{lo} monocytes express CC-chemokine receptor 2 (CCR2), which is involved in migration from the bone marrow to the bloodstream, and represent the main population of osteoclast precursors. Treatment with broad-spectrum antibiotics not only reduced gut inflammation in these rats, but also reduced the number of CD43^{lo} monocytes in the bone marrow and bloodstream to levels comparable with wildtype animals. High levels of CCL2, the ligand for CCR2, and IL-1α in the blood of HLA-B27 transgenic rats were also reduced by antibiotic treatment.

"The most significant finding of our study is the direct link between the gastrointestinal environment and how it moulds the central and peripheral myeloid compartment, which can contribute to the additional pathological aspects associated with spondyloarthropathies. Importantly, this includes controlling cellular distribution, migration, and differentiation," states Goodyear.

Joanna Collison

ORIGINAL ARTICLE Ansalone, C. *et al.* Gut inflammation in HLA-B27 transgenic rats alters the monocyte compartment and its osteoclastogenic potential. *Arthritis Rheumatol.* http://dx.doi.org/10.1002/art.40154 (2017)
FURTHER READING Ranganathan, V. *et al.* Pathogenesis of ankylosing spondylitis — recent advances and future directions. *Nat. Rev. Rheumatol.* **13**, 359–367 (2017)