Granulation Tissue Eroding the Subchondral Bone Also Promotes New Bone Formation in Ankylosing Spondylitis


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**SUMMARY**
New bone formation is a key feature of ankylosing spondylitis (AS). Previous histologic studies of joint material from AS patients suggested that a fibroblast-rich granulation tissue erodes the subchondral bone plate, which separates the bone marrow from the cartilage. This process is driven by osteoclasts. In an immunohistologic study of facet joints from AS patients, Bleil et al analyze whether this granulation tissue also has bone-forming capabilities. They show cells lining the granulation tissue, which express RUNX-2, CD56, and most importantly, type I collagen, identifying them as osteoblasts. No evidence of chondrocyte hypertrophy is seen. At contact zones between granulation tissue and cartilage, bony regions are observed, suggesting that successive bone generation at these sites promotes the bony bridging of the facet joints that is typical of AS.

**KEY POINTS**
- New bone formation leading to joint ankylosis and syndesmophyte development is typical of AS.
- Subchondral granulation tissue promotes destruction of the subchondral bone and cartilage in AS.
- Osteoblasts lining this granulation tissue promote ossification at borders between the granulation tissue and cartilage.
Interleukin-23–Dependent γ/δ T Cells Produce Interleukin-17 and Accumulate in the Enthesis, Aortic Valve, and Ciliary Body in Mice


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KEY POINTS
- Tissue-resident γ/δ T cells are present in uninflamed peripheral and axial entheses of mice.
- The γ/δ T cells are the main IL-17A–producing lymphocytes in the enthesal tissue and constitute the large majority of RORγt+ and IL-23R+ enthesis-resident T cells.
- Upon experimental IL-23 overexpression, enthesis-resident γ/δ T cells accumulate locally at sites of inflammation.

SUMMARY
Inflammation and ossification of entheses, the tendon–bone attachment sites, are hallmarks of the spondyloarthritides. It was previously reported that interleukin-23 (IL-23) drives this inflammation by triggering enthesis-resident retinoic acid receptor–related orphan nuclear receptor γt (RORγt)–positive and IL-23 receptor (IL-23R)–positive lymphocytes in mice. However, the role of γ/δ T cells in enthesal tissues has not yet been addressed. In this study, Reinhardt et al demonstrate that IL-17–producing γ/δ T cells with an activated Vγ6+CD27–RORγt+ phenotype are abundant in uninflamed enthesal tissues of mice. They show that there is constitutive expression of the IL-23R and that γ/δ T cells are the main IL-17A–producing lymphocytes at the enthesis. In an experimental model of minicircle DNA–induced IL-23 overexpression, mice developed inflammation of the paws, thickening of the aortic root and valve, inflammation of the eye, and psoriatic skin lesions, as well as local accumulation of γ/δ T cells at sites of inflammation, suggesting that γ/δ T cells are important players in the pathogenesis of IL-23–induced enthesal inflammation.