OSTEOARTHRITIS

The hedgehog and the bony spur

A new mouse study has revealed that inhibiting the smoothened (Smo) component of the hedgehog pathway curbs the development of bony spurs (osteophytes) in a serum transfer model of inflammatory arthritis. Importantly, this approach does not cause either local or systemic bone damage, because it does not block crucial mediators of physiological bone turnover (such as Wnt proteins), inhibition of which can increase the risk of osteoporosis and bone erosion.

Ruiz-Heiland *et al.* treated the mice with LDE223, a specific small-molecule inhibitor of Smo, for 2 weeks after the onset of arthritis. Smo is a key component of the hedgehog pathway, which controls embryonic bone growth through promoting endochondral ossification and the proliferation of chondrocytes. LDE223 had no influence on clinical signs of arthritis, such as body weight, swelling and grip strength. Similarly, Smo blockade did not reduce the area of inflammation in the synovium, or influence macrophage, neutrophil or lymphocyte expression.

However, animals treated with LDE223 had significantly reduced osteophyte development compared with untreated mice. Furthermore, the number of hypertrophic chondrocytes, which are important drivers of bone apposition in arthritis, was significantly reduced in LDE223-treated mice compared with control animals (8.60% versus 15.22%). Thus, Smo blockade might normalize irregular bone formation through blocking the formation of hypertrophic chondrocytes.

The results of this study provide early evidence that selective blockade of the hedgehog pathway might be a viable strategy to prevent osteophyte formation in patients with arthritis without inducing bone loss.

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Original article Ruiz-Heiland, G. *et al.* Blockade of the hedgehog pathway inhibits osteophyte formation in arthritis. *Ann. Rheum. Dis.* doi:10.1136/ard.2010.148262