Role of nerve growth factor and tropomyosin receptor kinase A in the pathogenesis of osteoarthritis. Might nerve growth factor be the link interwinding obesity and osteoarthritis?

We read with interest the paper by Nwosu et al recently published in Annals of the Rheumatic Diseases. They clearly provided evidence that blocking tropomyosin receptor kinase A (TrkA), the p140 high-affinity receptor of nerve growth factor (NGF), by a selective TrkA inhibitor AR786 relieves pain in two different rat models of osteoarthritis (OA). A reduction of synovitis was also shown by histopathology, suggesting that NGF inhibition exerted its effect at peripheral level on extraneural tissues. Authors concluded that inhibition of NGF activity might be an effective strategy as treatment of OA pain. Indeed, NGF may have pleiotropic effects, and we would like to speculate on being adult cartilage aneural, it is conceivable that it is not linked to perception of pain or other nervous system-related functions. Like in other cells, NGF might interact with growth factors and cytokines such as tumour necrosis factor (TNF)alpha and transforming growth factor (TGF)β-1, whose role in the pathophysiology of cartilage has been extensively studied. Although Nwosu et al did not detect any impact on cartilage in OA rats by TrkA inhibition, we believe the TrkA/NGF targeting may represent a promising strategy in the treatment of OA, including pain.

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Citation: Nwosu LN, Mapp PI, Chapman V, et al. Blocking the tropomyosin receptor kinase A (TrkA) receptor inhibits pain behaviour in two rat models of osteoarthritis. Ann Rheum Dis 2015;74:201420720 (Basic and translational research)

Competing interests None declared.

Provenance and peer review Not commissioned; internally peer reviewed.

Accepted 2 September 2015
Published Online First 18 September 2015

http://dx.doi.org/10.1136/annrheumdis-2015-208523


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4 Bulló M, Peerauly MR, Trayhurn P, et al. Circulating nerve growth factor levels in obese women correlate with body mass index (BMI) and in an increase in NGF plasma levels in obese women correlating with body mass index (BMI) and inflammatory markers was also reported.4 We are focusing on possible inter-relations between cartilage damage, BMI and NGF in human OA.5 We analysed knee articular cartilage from 19 obese patients with OA (13 female, BMI 31–37 kg/m2, age 41–84 years) and 10 normal-weight patients with OA (six female, BMI 21–23 kg/m2, age 28–73 years). Cartilage injury was assessed by Osteoarthritis Research Society International (OARSI) score6 and NGF expression by semiquantitative immunohistochemistry and real-time quantitative reverse-transcriptase polymerase chain reaction (RTQ-PCR) analysis. We found a significant correlation between OARSI score and BMI (r=0.64, 95% CI 0.35 to 0.82). Immunohistochemistry showed a correlation between NGF expression and BMI (r=0.76, 95% CI 0.53 to 0.88) or OARSI score (r=0.82, 95% CI 0.65 to 0.91). These findings were confirmed by RTQ-PCR analysis.

The role of NGF in chondrocyte metabolism is unknown, but being adult cartilage aneural, it is conceivable that it is not