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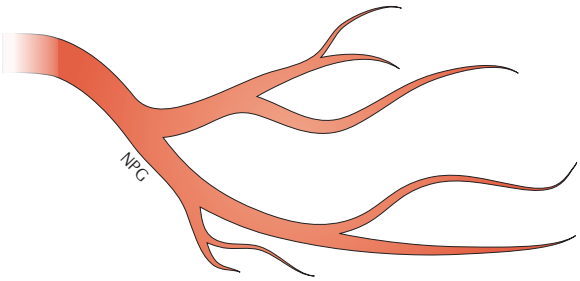
RHEUMATOID ARTHRITIS

CCN1, a novel RA target?

> CCN1 is an important … cytokine in rheumatoid arthritis

Protein CYR61 (cysteine-rich angiogenic inducer 61, also known as CCN1) is an important pro-inflammatory cytokine in rheumatoid arthritis (RA), according to new evidence published by Taiwanese researchers. They found elevated levels of CCN1 in synovial fluid from patients with RA, and showed that in mice with collagen-induced arthritis, a model of RA, knockdown of CCN1 (using a short hairpin RNA delivered by a lentiviral vector) suppressed joint swelling and cartilage erosion.



Interestingly, knockdown of CCN1 also blocked the production of vascular endothelial growth factor (VEGF) by osteoblasts, leading to suppression of pannus neovascularization and decreased expression of angiogenesis markers. "Our work also demonstrates a link between osteoblasts and angiogenesis in RA," highlights Chih-Hsin Tang, corresponding author of the study. "We provide evidence showing that osteoblasts produce VEGF and promote endothelial progenitor cell (EPC) infiltration and angiogenesis in the joint microenvironment during RA," he explains.

"This study reveals two major mechanisms through which CCN1 stimulates EPC-dependent angiogenesis," comments Zoltán Szekanecz, who was not involved in the study. Specifically, he notes, "CCN1 inhibits the microRNA miR-126, which is a potent VEGF inhibitor, inhibitor of angiogenesis and tumour suppressor. Thus, inhibition of miR-126 indirectly stimulates angiogenesis. CCN1 also directly increases VEGF expression in and production by osteoblasts."

Tang concludes, "Our findings offer insights into the cellular and molecular interactions involved in skeletal remodelling, which may prove beneficial in the ongoing search for potential therapeutic targets in arthritis." And Szekanecz concurs: "As CCN1 is involved in both synovial inflammation and angiogenesis, it may indeed be a target for therapy using an antibody or a small-molecule inhibitor."

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ORIGINAL ARTICLE Chen, C.-Y. *et al.* CCN1 promotes VEGF production in osteoblasts and induces endothelial progenitor cells angiogenesis by inhibiting miR-126 expression in rheumatoid arthritis. *J. Bone Miner. Res.* http://dx.doi.org/10.1002/jbmr.2926 (2016)
FURTHER READING Vicente, R. *et al.* Deregulation and therapeutic potential of microRNAs in arthritic diseases. *Nat. Rev. Rheumatol.* **12**, 211–220 (2016)