Clinical Connections

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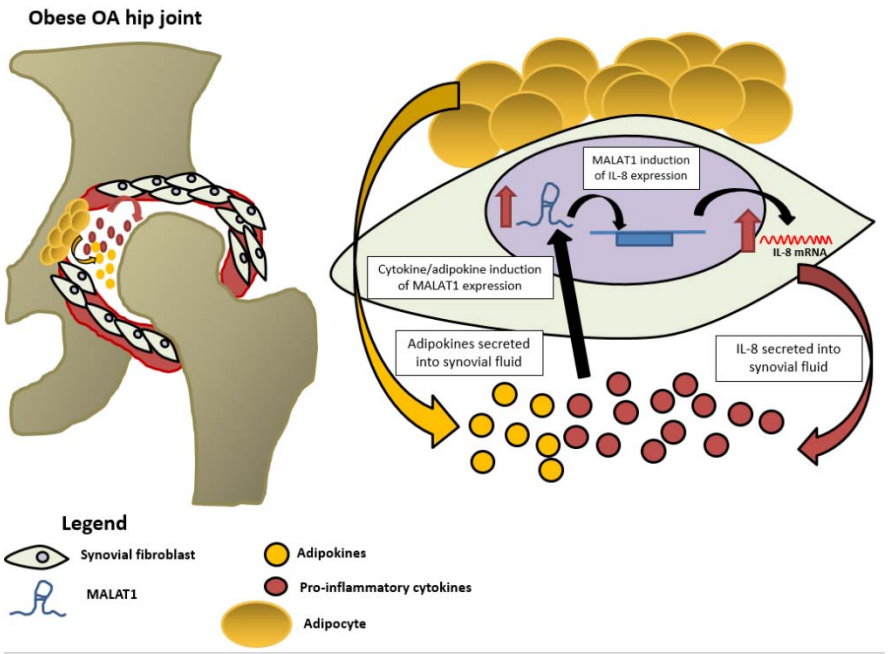
Regulation of the Inflammatory Synovial Fibroblast Phenotype by MALAT 1 LncRNA in Obese Patients with Osteoarthritis

Summary:

Inflammation and enlargement of the synovium (synovitis) is a central pathological feature of osteoarthritis (OA). Nanus et al find synovitis is greater in hip OA patients who are obese, where the synovial fibroblast cells (SF) exhibit an inflammatory phenotype with increased production of pro-inflammatory cytokines such as interleukin-6 (IL-6) and C-X-C Motif Chemokine Ligand 8 (CXCL8), compared to either normal weight OA individuals or non-disease controls.

The inflammatory synovial fibroblast phenotype is associated with the expression of specific long non-coding RNAs (lncRNAs), a new class of gene regulators. The lncRNA MALAT1 is rapidly produced in OA SF cells in response to inflammatory stimulation with pro-inflammatory cytokines. Inhibition of MALAT1 reduces the rate of SF cell growth and decreases the production and release of inflammatory proteins. These findings demonstrate that obese hip OA patients have an inflammatory synovial fibroblast phenotype and that MALAT1 lncRNA is a central regulator in mediating synovitis in OA patients who are obese.



Key Points:

- Synovial fibroblasts from obese OA patients have an inflammatory phenotype
- The inflammation-associated lncRNA MALAT1 is highly abundant in obese OA synovial fibroblasts and is rapidly produced in response to inflammatory cytokine stimulation
- Inhibition of MALAT1 reduces the synovial fibroblast inflammatory phenotype by inhibiting the production of inflammatory cytokines
- Targeted inhibition of MALAT1 could be a therapeutic approach to reducing synovitis in obese OA patients