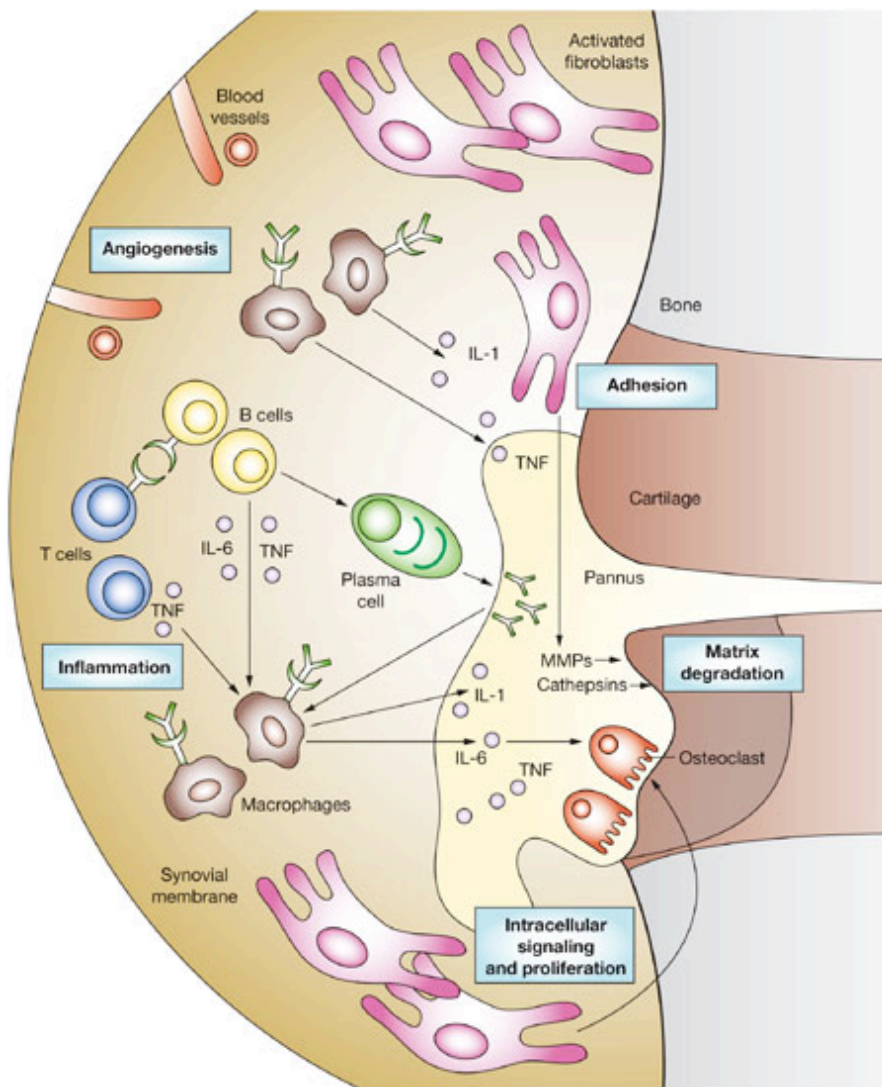


# Lecture 23. Rheumatoid Arthritis

## Learning Objectives and Summary



### Pathways involved in inflammation and destruction in the rheumatoid joint

The five key factors of intracellular signaling and proliferation, adhesion, inflammation, angiogenesis, and matrix degradation are linked by various inflammatory effector cells, such as tumor necrosis factor, interleukin-1 and interleukin-6, and matrix-degrading enzymes, including matrix metalloproteinases and cathepsins, finally resulting in a persisting vicious circle. IL, interleukin; MMPs, matrix metalloproteinases; TNF, tumor necrosis factor. From: Muller-Ladner et al., *Nature Clin. Practice Rheumatol.* 1:102, 2005

## 23. Rheumatoid Arthritis

### Learning objectives:

1. To understand the clinical features of Rheumatoid Arthritis (RA)
2. To understand proposed pathophysiologic mechanisms that result in the inflammation and pathology of RA.
3. To understand the principles behind current and future therapy of RA

### SUMMARY

1. RA is a chronic, inflammatory autoimmune disease characterized by articular and extra-articular clinical manifestations.
2. Autoreactive antibodies in RA include rheumatoid factor and anti-CCP (cyclic citrullinated peptide) antibodies.
3. Autoreactive T cells, B cells, and an inflammatory cytokine milieu contribute to the immunopathology of RA.
4. The pannus is a membrane of granulation tissue covering the normal surface of the articular cartilages in rheumatoid arthritis. It consists of proliferating synoviocytes, infiltrating T cells, B cells, and plasma cells. Th1 cytokines are abundant in the pannus and play a role in promoting joint destruction. Other factors that promote pannus formation include MMPs, RANK-L (an osteoclast pro-survival factor), and pro-inflammatory cytokines released from macrophages, especially TNF- $\alpha$  and IL-1.
5. Treatment of RA is directed at inhibition of pro-inflammatory products from macrophages and T cells (e.g., NSAID, TNF inhibitors, IL-1 antagonists), inhibition of lymphocyte or synovial proliferation (methotrexate, azathioprine), inhibition of T cell activation and function (cyclosporin, gold, corticosteroids).
6. New approaches to the treatment of RA include inhibition of co-stimulation (CTLA4-Ig, anti-CD40L) and B cell depletion (Rituximab).