

## **Seed/Walsh (eds): Angiogenesis in Inflammation – Mechanisms and Clinical Correlates**

### **Summary**

**Paul I. Mapp and David A. Walsh**

#### **Neurogenic angiogenesis and inflammation**

Stimulation of unmyelinated sensory nerve fibres produces a local response termed 'neurogenic inflammation'. This neurogenic inflammation is mediated by biologically active neuropeptides. This chapter explores the role of these neuropeptides in the induction, or suppression, of angiogenesis in both the acute and chronic inflammatory condition. An hypothesis is advanced which suggests that there is a handover of roles from one peptide to another dependent on whether the situation is acute or chronic. Manipulation the neuronal regulation of vascular growth may offer potential therapies in inflammatory conditions.

### **Summary**

**Peter C. Taylor**

#### **The angiogenic drive in chronic inflammation: hypoxia and the cytokine milieu**

Many angiogenic factors are expressed in chronic inflammatory conditions such as RA, as well as indices of hypoxia such as HIF transcription factors. Despite the increased vascularity associated with RA synovitis, the RA joint is hypoxic. Repetitive cycles of hypoxia and reoxygenation together with oxidants produced by phagocytic cells promote chronic oxidative stress within the microenvironment of the joint leading to generation of reactive oxygen species with the potential to cause tissue damage. Changes in cellular oxygenation regulate intracellular concentrations of the transcription factor HIF-1 $\alpha$  that activates a gene program permissive to perpetuation of synovitis.

### **Summary**

**Elena Riboldi, Silvano Sozzani and Marco Presta**

#### **Dendritic cells and angiogenesis**

Dendritic cells (DC) are professional antigen presenting cells that play a pivotal role in the onset and regulation of adaptive immune responses. Also, DC share with other phagocytes the ability to regulate inflammation through their ability to release cytokines and chemokines and kill pathogens. Recent observations have shown that different DC subsets produce and release various pro- and anti-angiogenic mediators depending upon their activation status and the cytokine milieu. In particular, alternatively activated DC exert a potent pro-angiogenic activity that is mediated by the prototypic angiogenic growth factor Vascular Endothelial Growth Factor (VEGF). In turn, pro- and anti-angiogenic mediators can affect the biology of DC modulating their differentiation and maturation. Finally, DC can differentiate into endothelial-like cells. Thus, DC may exert an important impact on the neovascularization process in different physio-pathological conditions.

**Keywords:** angiogenesis, cancer, cytokines, chemokines, dendritic cells, endothelial cells, immunity, inflammation, interferon, leukocytes, monocytes, prostaglandins, thrombospondin, trans-differentiation, tissue repair, vasculogenesis, VEGF

**Ewa Paleolog and Mohammed Ali Akhavani**  
**The lymphocyte in inflammatory angiogenesis**

**Summary**

**Patrick Auguste, François Vincent, Giulio Gabbiani and Alexis Desmoulière**  
**The fibroblast and myofibroblast in inflammatory angiogenesis**

The role of fibroblastic cells, including myofibroblasts, in tension production and extracellular matrix synthesis during inflammatory and fibrotic phenomena is well established. In addition, it is more and more accepted that myofibroblasts are involved in other crucial events during these phenomena, such as cell-cell and cell-matrix communication or angiogenesis. Here, we review the mechanisms of myofibroblast participation to inflammatory and fibrotic angiogenesis. It appears that this cell plays a complex pivotal role in the mechanical and biological organization of angiogenesis during the development of pathological fibrous tissue, including stroma reaction to epithelial tumors. The understanding of the mechanisms of these phenomena may yield new therapeutic strategies concerning several pathological situations.

**Keywords:** myofibroblast,  $\alpha$ -smooth muscle actin, granulation tissue, vascular endothelium growth factor, stroma reaction, fibrosis, cirrhosis, liver sinusoid, hepatic stellate cell, renin, angiotensin, angiotensin-converting enzyme

**Zoltán Szekanecz and Alisa E. Koch**  
**Chemokines and cytokines in inflammatory angiogenesis**

**Keywords:** angiogenesis, chemokines, inflammatory chemokines, chemokine receptors, cytokines, rheumatoid arthritis

**Chandan A. Alam, Paul Colville-Nash and Michael P. Seed**  
**Modeling angiogenesis in inflammation**

**Summary**

**David A. Walsh and Eirlys Williams**  
**Angiogenesis in the inflammation of arthritis**

The human joint is a complex, highly evolved structure comprising soft and hard tissues, both vascular and avascular. Joint inflammation (arthritis) is a major burden for which current treatments are palliative, rather than curative. Inflammation and angiogenesis may be observed within the arthritic synovium and its growing and invasive pannus, at tendon insertions, and within subchondral bone and osteophytes, in each of which they may contribute to symptoms and joint damage. Understanding the bidirectional link between inflammation and angiogenesis may lead to novel therapies for a wide variety of joint diseases, including rheumatoid arthritis and osteoarthritis. Anti-angiogenic strategies reduce inflammation and joint damage in animal models of arthritis. Of key importance will be

whether inhibition of angiogenesis can reduce other symptoms and signs of inflammation; pain, stiffness and swelling. The development of anti-angiogenic treatments in non-rheumatological fields of medicine such as oncology raises hope for a group of conditions which cause widespread disability and distress.

**Keywords:** rheumatoid arthritis, osteoarthritis, psoriatic arthritis, ankylosing spondylitis, bone, cartilage, synovium, ligament, tendon, pain

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