TNF-α AND TNF-α-INHIBITION IN WOUND HEALING

Marcus Streit

Kantonsspital Aarau, Aarau, Switzerland

TNF-α is a 157-amino acid, 17kDa protein that acts as a cytokine in a wide variety of cellular activities. TNF-α is produced by monocytes and macrophages but also by many other cells. Its receptors can be found on almost every cell.

In inflammation TNF-α acts as a proinflammatory cytokine and plays a principle role in a number of inflammatory diseases. Due to its role in many pathophysiological conditions TNF-α has become an interesting target for therapy of many diseases. Commercially available monoclonal antibodies (infliximab, adalimumab) or fusion proteins (etanercept) can be used to inhibit TNF-α. Today, TNF-α-inhibitors are widely used to treat inflammatory diseases, e.g. rheumatoid arthritis, Crohn’s disease or psoriasis. But also in inflammatory skin diseases that cause cutaneous ulceration, e.g. pyoderma gangraenosum or vasculitis, TNF-α-inhibitors have proven to be effective.

In normal wound healing TNF-α is involved in all stages of healing, especially in the inflammatory phase. It is controversially discussed whether TNF-α has a stimulatory or inhibitory effect on wound healing, but it seems that an exceeding amount of TNF-α inhibits wound healing: In human chronic wound fluids high levels of TNF-α are associated with non healing wounds.

In vitro studies have demonstrated that TNF-α directly stimulates the synthesis of matrix metalloproteinases (MMPs) in fibroblasts. Increased activity of MMPs is suggested to be a key factor for the chronicity of wounds. Persisting high levels of proinflammatory cytokines in chronic wounds could be responsible for increased activity of MMPs and non-healing wounds. Therefore inhibition of TNF-α should be beneficial for wound healing. Clinical observations demonstrated that inhibition of TNF-α led to rapid healing of chronic wounds of different etiologies. Inhibition of TNF-α might become a therapeutical option for difficult to heal chronic wounds.