Suppression of Neutrophil-Mediated Tissue Damage – A Novel Skill of Mesenchymal Stem Cells

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Neutrophils, if overactivated, can cause severe tissue damage in neutrophilic dermatoses such as pyoderma gangrenosum, immune-complex mediated vasculitis and chronic venous leg ulcers, disorders with remarkable morbidity which often poorly respond to conventional therapies. Mesenchymal stem cells exert beneficial effects on chronic wounds by dampening unrestrained inflammation of both adaptive and innate immune cells. Though of prime clinical importance the effects of MSCs on neutrophils so far have not been studied in sufficient detail. Therefore, we set out to investigate the effects of human adipose tissue derived MSCs on neutrophil activation.

**Conclusion:**

MSCs reduce cell death, oxidative burst, protease release and NET formation in cocultured neutrophils. MSCs reduce ROS release in a mouse model of acute skin inflammation. Over-activated neutrophils mediate tissue damage in vasculitis patients. MSCs reduce hemorrhage and tissue destruction of IC-mediated vasculitis in mouse skin. MSCs reduce cell death and oxidative burst of neutrophils, and suppress release of active neutrophil enzymes and NET formation in vitro. MSCs reduce the severity of tissue damage in mouse models of acute skin inflammation and immune complex-mediated vasculitis in vivo. MSCs are found to engulf apoptotic neutrophils in an ICAM-1 dependent manner and adaptively release higher level of SOD3 in response to the elevated ROS level from over-activated neutrophils, to protect the tissue homeostasis.