

# **Molecular Oxygen and Reactive Oxygen Species in Tissue Repair – New Insights in the Good, the Bad and the Ugly**

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The state of wound oxygenation and derivatives of molecular oxygen including distinct entities of reactive oxygen species are critical key determinants in tissue repair and - if dysregulated - result in severe developmental and healing deficiencies. Molecular oxygen is essentially required for ATP synthesis for the enhanced demands of tissue restoration, however, in early inflammatory wound healing phases much of the molecular oxygen is channelled into the NADPH oxidase-dependent superoxide anion radical release which in initial phases of wound healing is necessary to combat bacterial infections at the wound site and has a role in angiogenesis. Under physiological conditions superoxide anion radicals are dismutated to hydrogen peroxide which plays an important role in redox-signalling and in the prolongation of growth factor signaling. However, too little and too much of either molecular oxygen and distinct oxygen species delays development and results in chronic wounds which do not properly progress through different wound healing phases and remain stuck in the late inflammatory phase with little and no tendency to heal. We recently identified the iron-macrophage to be the key player responsible for the sustained non-healing stage of chronic venous leg ulcers and most likely also diabetic foot ulcers. Accumulation of iron derived from extravasated erythrocytes is responsible for the unrestrained activation of pro-inflammatory M1 macrophages and enhanced release of superoxide anion radicals into the wound bed of chronic venous leg ulcers, and most likely other macrophage dominated diseases like arteriosclerosis, Parkinson's disease and multiple sclerosis. Superoxide anions at persistent high concentrations result in Insulin-like Growth Factor-1 resistance further impeding tissue repair. I will discuss how to translate these findings into therapeutic concepts within the frame of current treatment strategies.