

# **Elucidation of therapeutic effect and regulatory mechanism of mesenchymal stem cells on oxidative stress disorder of skin**

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Cutaneous ischemia-reperfusion (I/R) injury is associated with the early pathogenesis of cutaneous pressure ulcers (PUs). The objective of this study was to investigate the effect of mesenchymal stem cells (MSCs) injection on the formation of PUs after I/R injury and determine the underlying mechanisms. We found that the subcutaneous injection of MSCs into areas of I/R injured skin significantly suppressed the formation of PUs. I/R-induced vascular damage, hypoxia, oxidative DNA damage, and apoptosis were decreased by MSCs injection. Oxidative stress signals detected after I/R in OKD48 (Keap1-dependent oxidative stress detector, No-48-luciferase) mice were decreased by the injection of MSCs. In cultured fibroblasts, MSCs-conditioned medium significantly inhibited oxidant induced reactive oxygen species (ROS) generation and apoptosis. Furthermore, endoplasmic reticulum (ER) stress signals detected after I/R in ERAI (ER stress-activated indicator) mice were also decreased by the injection of MSCs. These results suggest that the injection of MSCs might protect against the development of PUs after cutaneous I/R injury by reducing vascular damage, oxidative cellular damage, oxidative stress, ER stress, and apoptosis.