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INVITED CRITIQUE

The Future of CACs in Wound Healing

This seminal article by Zhang et al demonstrates the crucial role of CACs in delayed healing in general and in burns in particular. This report advances research in the wound field in that it provides a unique model that demonstrates a similar physiologic response of CACs in burned mice and in human patients with burn injuries. Despite the dissimilarities in magnitude and duration of CAC mobilization between the 2 populations, the authors demonstrate the importance of the study of CAC mobilization in the experimental and human groups.

Zhang and colleagues have developed a superior burn wound–healing model that correlated angiogenic response to the depth of the burn. By precisely regulating burn depth, they found a delay in mobilization of CACs, exemplified by the progressive decrease in peak mobilization correlated with increasing burn duration. This model allows researchers in the field to investigate the contribution of injury not only to direct tissue destruction but also to its effect on wound angiogenesis. This is demonstrated by the significant immunohistochemical finding of decreased numbers of CD31- and SMA-positive vessels observed with increased burn duration.

Experimental models have previously demonstrated the contribution of CACs in the repair of endothelial function and reduced neointimal formation after arterial injury. In one study,[1] lipopolysaccharide-induced endothelial injury in rats demonstrated a 40% decrease in endothelial cells, which returned to normal after 24 hours. This finding was correlated with a 3-fold increase in the percentage of CACs, supporting the hypothesis that endothelial injury caused by inflammation activates CAC mobilization. Although the mechanisms of activation and mobilization have yet to be fully elucidated in humans, it is evident that CACs maintain a crucial role in the inflammatory response through their effect on angiogenesis and vascular repair.[2]

Although extensively studied in the cardiovascular and burn fields, the contribution of CAC advances has the potential to be applicable to multiple types of wounds in which decreased angiogenesis is present, such as diabetic[3] and ischemic[4] ulcers. Furthermore, no biological treatment is currently available for pressure ulcers in the United States. Because these wounds have been associated with ischemic injury and the subsequent cytokine response,[5] they may very well benefit clinically from CACs.

One unanswered question concerns the most optimal method for stimulating CAC mobilization at the site of the wound in patients to increase the angiogenic and healing response. Future work will be needed to bring angiogenic cell therapy to the clinic for burn-injured patients and potentially other patients with chronic wounds.

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