Extremity Trauma Rehabilitation and Treatment

Evaluation of Next Generation Regenerative Medicine Therapeutics and Approaches for the Restoration of Tissue Structure and Function Following Traumatic Injury

War-related trauma often results in complex, composite tissue injuries which can result in persistent functional deficits, chronic disability, and reduced quality of life (QOL). To address this unmet clinical need, the regenerative medicine field has made significant efforts in recent years toward the development of innovative short- and long-term solutions. A focus of the Extremity Trauma and Amputation Center of Excellence (EACE) Medical/Surgical Interventions line of inquiry at the Walter Reed National Military Medical Center (WRNMMC) and Uniformed Services University of the Health Sciences (USUHS) is the evaluation of next generation regenerative medicine therapeutics and approaches for the restoration of tissue structure and function following traumatic injury. This is particularly relevant for Service Members and Veterans with extremity trauma and/or amputation. Three studies were published by EACE staff in this line of research:

The first study reports on the role of a biologic scaffold material, urinary bladder matrix (UBM), in wound care and reconstruction of traumatic and combat wounds.[1] The UBM, an acellular, non-cross-linked, resorbable, biologically-derived extracellular matrix scaffold, was found to facilitate definitive soft tissue reconstruction by establishing a neovascularized soft tissue base acceptable for second stage wound and skin coverage options within traumatic and combat-related wounds. This study demonstrates that the use of a regenerative medicine therapeutic in conjunction with other reconstructive techniques can be a successful adjunct in the reconstructive algorithm for complex traumatic wound reconstruction and limb salvage procedures.

The second study was undertaken to further understand the impact of the manufacturing process on the ability of a regenerative medicine technology to facilitate tissue reconstruction.[2] Specifically, the objective of this study was to elucidate the most effective yet minimally destructive sterilization protocol for a biologic scaffold material. Three different sterilization methodologies - ethylene oxide, gamma irradiation, and electron beam irradiation – were evaluated for their effect on the material properties of a porcine dermal biologic scaffold and the elicited in vivo remodeling response. In vitro results show that increasing irradiation dosage resulted in a dose dependent decrease in mechanical properties compared to untreated controls. The study showed that increasing levels of irradiation induced an adverse effect on the material properties and augmented the remodeling response both in vitro and in vivo. These findings highlight the importance of selecting an appropriate type and dose of sterilization for biologic scaffold materials to optimize their material properties and performance in vivo.

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1 Valerio, I. L., Campbell, P., Sabino, J., Dearth, C. L., & Fleming, M. (2015). The use of urinary bladder matrix in the treatment of trauma and combat casualty wound care. Regenerative Medicine, 10(5), 611–622. https://doi.org/10.2217/rme.15.34

2 Dearth, C. L., Keane, T. J., Carruthers, C. A., Reing, J. E., Huleihel, L., Ranallo, C. A., … Badylak, S. F. (2016). The effect of terminal sterilization on the material properties and in vivo remodeling of a porcine dermal biologic scaffold. Acta Biomaterialia, 33, 78–87. https://doi.org/10.1016/j.actbio.2016.01.038

The third study investigated the effect of aspirin on the ability of a biologic scaffold material to facilitate skeletal muscle tissue reconstruction following injury.[3] The findings suggest that aspirin can negatively impact the repair/regeneration events elicited by biologic scaffolds in a skeletal muscle injury model. Additional work must be conducted to determine if these deleterious effects of aspirin will irreparably reduce the regenerative response or simply delay it. The results of the current work not only provide a better understanding of the mechanisms involved in biologic scaffold mediated constructive remodeling and begin to classify molecular targets to be used as metrics for the development of next generation biologic scaffolds, but also substantiate the possibility that the use of non-steroidal anti-inflammatory drugs may significantly alter tissue remodeling outcomes in regenerative medicine/tissue engineering applications.

3 Dearth, C. L., Slivka, P. F., Stewart, S. A., Keane, T. J., Tay, J. K., Londono, R., … Badylak, S. F. (2016). Inhibition of COX1/2 alters the host response and reduces ECM scaffold mediated constructive tissue remodeling in a rodent model of skeletal muscle injury. Acta Biomaterialia, 31, 50–60. https://doi.org/10.1016/j.actbio.2015.11.043