Treatment Strategies

Mesenchymal Progenitor Cell Therapy to Prevent Muscle Fibrosis

Recent military conflicts in Iraq and Afghanistan (Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF)) have resulted in a number of military casualties with a disproportionately large number of orthopedic injuries. These traumatic extremity injuries are in many ways unique when compared to their civilian equivalents because of the associated tissue loss and dysfunction. In the scenario of devastating tissue destruction, the body's first response is to heal itself and repair or regenerate damaged or missing tissue. The repair process tries to prepare the microenvironment for the creation of a functional tissue. However, if the microenvironment is not biologically favorable for functional tissue creation, then a non-functional, tissue-void filler is produced (known as scar tissue) and the tissue repair mechanisms are attenuated. Once the microenvironment changes from one of wound healing (tissue repair and regeneration) to that of wound closure (scar formation) the previously biologically active wound bed becomes less active and the scar tissue actively contracts in an effort to close the wound.

This study was funded by the Defense Medical Research and Development Program (DMRDP), managed by the Congressionally Directed Medical Research Program (CDMRP), and conducted at the National Intrepid Center of Excellence (NICoE). Tissue samples were obtained from Service Members who have been wounded in combat and are undergoing surgical debridement at Walter Reed National Military Medical Center (WRNMMC). The purpose of this study was to demonstrate that mesenchymal progenitor cells (MPCs)/trauma induced stem cells isolated from war-time extremity injuries are similar to mesenchymal stem cells (MSCs). One notable and significant advantage of MPCs is that the MPC population found in traumatic wounds is approximately 10,000 times more plentiful than the MSC population found in bone marrow. Using the clinical samples collected from WRNMMC, the study team has established the optimized parameters for the MPC/trauma induced stem cell harvesting procedure and completed a safety analysis of the harvesting method that can be used as justification for a future Phase 2 clinical trial. In addition, using an in vivo rat model, the effectiveness of MPC/trauma induced stem cell therapy to prevent dysregulated healing, exuberant scar formation, and muscle fibrosis and contracture following traumatic injury has been demonstrated.

Wartime traumatic extremity injuries are in many ways unique when compared to civilian equivalents because of the associated tremendous tissue loss and dysfunction. Often times the tissue is damaged beyond repair or involves a significant segmental defect rendering it non-functional. After thorough surgical debridements, the critical decision of whether to pursue limb salvage versus amputation needs to be made. The significant increase in availability of MPCs make them a practical choice for tissue engineering and regenerative medicine applications, especially if harvested in the same surgical setting that a reconstructive procedure will be performed. It is believed that these cells are central to tissue repair and regeneration and have the potential to augment wound healing through contributing to functional tissue repair. The knowledge gained from these experiments will lead to novel cellular therapies that are feasible for military medical centers. Our strategy has the potential to improve the outcome of wounded Service Members resulting in an increased return to service rate, improvement in active duty retention rate, and reduction in long-term disability rates.