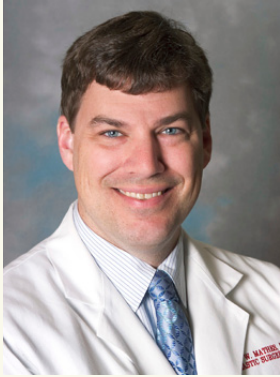


## David Mathes, MD Awarded AFIRM II Funds



David W. Mathes, MD

On September 27, 2013, the US Army Medical Department announced \$75 million in funding for the Armed Forces Institute of Regenerative Medicine: Warrior Restoration Consortium (AFIRM II). We are pleased to announce that The University of Washington was awarded \$1.2 million over five years for this project. The UW joins a 30-plus member

consortium working on areas of regenerative medicine. **Dr. David W. Mathes**, Associate Professor of Surgery in the Division of Plastic Surgery, is the PI for the UW portion of AFIRM II. His team will be conducting research on *“Tolerance Induction to Vascularized Composite Allografts in a Pre-Clinical Large Animal Model.”*

The 5-year AFIRM II program continues AFIRM I, which was established in 2008 and focused on regenerative medicine that developed therapies for severely wounded US service members. AFIRM funds basic through translational regenerative medicine research. Regenerative medicine technologies present many unique opportunities for the treatment of combat-related traumatic injury as well as benefits to those within the civilian sector. AFIRM’s goal is to position promising technologies for entrance into human clinical trials.

One of the 5 major focus areas for AFIRM II and the one Dr. Mathes’ project team will focus on, is vascularized composite allografts (VCA). Conventional reconstructive procedures used for treating major tissue loss have been largely inadequate when reconstructing severe extremity injuries, such as a lost hand or repairing devastating injuries to the face. Conventionally reconstructed patients require multiple revision procedures, endure prolonged rehabilitation and still frequently suffer from poor functional outcomes and donor site morbidity.

VCA represents a significant advancement in reconstructive surgery, offering the opportunity to replace lost tissue with the exact same tissue taken from a donor. VCA reconstructive surgery results in improved cosmetic and functional outcomes while significantly decreasing the need for multiple revision surgeries. To date, over 70 hand allografts have been transplanted worldwide with survival times reported up to 15 years post-transplant. More recently,

over 20 patients have undergone transformational facial transplantation surgeries.

However, as with all transplants, survival of the VCA is dependent on chronic immunosuppression. Prolonged immunosuppression negatively impacts quality of life, alters the risk profile and may jeopardize the benefits gained from a transplant. This is where Dr. Mathes and his team are focusing their research.

Previously, in collaboration with **Dr. Rainer Storb**, Head of the Transplantation Biology Program at Fred Hutchinson Cancer Research Center (FHCRC) and Staff Scientist Scott Graves, PhD, Dr. Mathes developed a pre-clinical large animal model for VCA. He used this clinically relevant model to apply a technique of non-myeloablative bone marrow transplantation (pioneered at the FHCRC), to induce immunologic tolerance to the allograft. Recently his group successfully demonstrated that the simultaneous transplantation of mobilized hematopoietic stem cells and a vascularized composite allograft leads to tolerance to VCA across minor antigen barriers for greater than one year. During this and subsequent work, the team observed that tolerance to the allograft could occur without the need for long-term engraftment of the stem cell transplant.

Based on these observations, Dr. Mathes’ 5-year AFIRM II project will focus on the development of immunologic tolerance to VCA, undertaking experiments to determine whether a transient hematopoietic stem cell graft is sufficient for the VCA to be permanently accepted. The overall strategy involves co-transplantation of HCT to generate a state of donor cell “chimerism” via non-myeloablative HCT. This state of donor cell chimerism appears to induce the production of regulatory T-cells that allow these transplants to be maintained without the need for immunosuppression. Dr. Mathes and his team will also examine the mechanisms involved in tolerance induction with a special focus on T-regulatory cells and their associated chemokines.

The ultimate goal of this work is to develop a protocol that can be applied to human hand and face transplants across all genetic barriers. Eliminating the need for chronic immunosuppression will significantly impact the risk-benefit ratio of VCA and allow for more widespread use of this revolutionary reconstruction technique.

Source: Armed Forces Institute of  
Regenerative Medicine / <http://www.afirm.mil/>