

Exploring the promise of stem cells for reconstruction

Editor's note: This is the first in a multi-part series highlighting each of the 2008 National Endowment Grant Award winners and the research they are conducting to improve patient safety and develop new technologies for plastic surgeons.

THE RESEARCHER

Howard Wang, MD

Title: Assistant professor, program director and plastic surgery residency interim chief, Division of Plastic and Reconstructive Surgery, University of Texas Health Science Center, San Antonio



Project:

Neovascularization of Bony Constructs Using Adipose Tissue-Derived Stem Cells

PSN: What is the purpose of your project?

Dr. Wang: My interest is in finding ways of reconstructing patients through tissue engineering, thus lessening the need for an invasive donor site (i.e., harvesting stem cells). Tissue engineering of bony constructs presents a promising reconstructive option for large bony defects. While the use of bone allograft as a matrix has the advantage of immediate tensile strength, the porosity of polymer matrices is advantageous for cellular in-growth and nutrient diffusion. The formation of a vascular network is a key factor in the success of larger or less-porous bony constructs.

This neovascularization will ultimately need to be developed on both a macroscopic and microscopic level. The macroscopic level – involving vessels that can be used in a microvascular anastomosis – must give way to a capillary network capable of penetrating the dense connective matrix of bony tissue.

Adipose tissue-derived stem cells (ASCs), which can be isolated with minimal donor site morbidity, have the ability to differentiate into both osteoblasts and endothelial cells by culture in specific media. In addition, endothelial cells have the potential to populate a matrix and form capillary networks. Thus, ASCs provide an excellent cellular source for tissue-engineered constructs. Specifically, this project seeks to evaluate the ability of ASC-derived endothelial cells to populate and form capillary networks in both polymer and calvarial allograft scaffolds *in vitro*. We will also attempt to create bony constructs with viable osteoblasts and a capillary network by co-culturing ASC-derived osteoblasts and endothelial cells, in polymer and calvarial allograft scaffolds.

PSN: At what stage are you in your research?

Dr. Wang: We are setting up the lab and generating exciting preliminary data, so once the grant period starts, we will be able to complete our experiments in a timely manner. We have spent much time setting up the physical environment of the lab and servicing key pieces of technology that we will employ in the grant process. We also continue in collaboration with local researchers in tissue engineering in parallel projects, all in the hope of reaching our ultimate goal of clinical applicability of our data.

PSN: What will be the project's applicability?

Dr. Wang: Our goal is one of clinical rele-



Dr. Wang in the O.R.

vance. Ultimately, we would like to take a scaffold – whether biologic or synthetic – and populate it with the patient's own stem cells. This would allow us to generate tissue from a donor site *in vitro* with minimal morbidity.

Thus far, our models have relied on diffusion to keep osteoblasts alive, due to the thin nature of the tissue. However, with human bones, diffusion alone will not suffice; that's why we use free flaps or composite tissue allotransplantation to reconstruct complex wounds. With this set of experiments, we hope to reliably create a microvasculature in the scaffold to support cells that are distant from the source of nutrition, thus allowing us to create larger, more complex tissue for reconstructive purposes. Our ultimate goal

would be to take a patient's stem cells, create a bony construct *in vitro*, then implant this construct back into the patient for reconstruction.

PSN: What led you to embark on this project?

Dr. Wang: During my plastic surgery residency under L. Scott Levin, MD, and Detlev Erdmann, MD, at Duke University, Durham, N.C., I was able to participate in experiments using adipose-derived stem cells. I decided to continue with this line of research after my move to San Antonio in 2005 and I've been fortunate in having support from the University of Texas – and also in finding collaborators in the community who share a common interest.

PSN: What's next for your research?

Dr. Wang: We will need to first complete the PSEF

the ideal construct to seed our stem cells into.

PSN: Has this research affected or attracted other investigators in this field?

Dr. Wang: I'm amazed at the amount of interest in San Antonio in using adipose-derived stem cells. We are currently collaborating with two other research groups and producing some very exciting research. This collaboration will only help forward our eventual goals in a more efficient manner and certainly help avoid any duplication; rather, we will continue with our collaborators in a complementary fashion toward our goal of developing a construct in the *in vitro* setting that we can use for reconstructive purposes.

PSN: How will the PSEF grant take your research to the next level?

Dr. Wang: I think the PSEF grant and the research we will generate should go a long way in helping us secure further funding. Our eventual goal, as with any lab, is obtaining NIH funding down the line. More importantly, I hope our work will eventually lead to translatable results and give patients – and the field of plastic surgery – additional options in the reconstructive ladder.

project, of course. This will undoubtedly raise as many questions as it will answer. We're still working with a very thin bone model. For our research to be translatable to the clinical setting, we must go to long bone and larger animal models. Furthermore, once a micro-vasculature is developed, we still must find a way to connect it to the macrovasculature of the patient. As well, we will continue to explore different scaffolds – both biologic and synthetic – in order to learn which will be



Dr. Wang with research assistants and second-year plastic surgery residents David Sahar, MD, and Stacy Stephenson, MD, who Dr. Wang calls instrumental in his research endeavors.

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