Wound healing goes green | Science Translational Medicine

1. Kara L. Spiller

1. *School of Biomedical Engineering, Science, and Health Systems, Drexel University, Philadelphia, PA 19104, USA. E-mail: spiller@drexel.edu*

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Tissue engineering holds the potential to transform medicine through the creation of healthy tissues and organs that can replace or repair damaged body parts. However, a major challenge in the generation of large, complex tissues is maintenance of a sufficient supply of oxygen, which is required to keep the cells alive after implantation. Chavez *et al*. therefore engineered biomaterials capable of producing their own oxygen by incorporating photosynthetic microalgae. As a bonus, microalgae can be genetically engineered to secrete human growth factors to further promote tissue regeneration.

In a strategy the team calls HULK, German for "conditioning hyperoxia under light," photosynthetic *Chlamydomonas reinhardtii* cells were transformed to secrete human vascular endothelial growth factor (VEGF), a potent proangiogenic growth factor, and seeded the algae onto collagen scaffolds. After confirming the ability of the microalgae to secrete both oxygen and bioactive human VEGF in vitro, the constructs were implanted into skin defects of healthy, immunocompetent mice. Importantly, no overt immune response to the microalgae was noted, as evidenced by a lack of changes in lymphoid or nonlymphoid organ microstructure, leukocyte activation, or serum levels of inflammatory cytokines compared with controls. After 2 weeks of implantation, the microalgae enhanced scaffold vascularization and wound healing, with modest increases from the secretion of human VEGF. However, it was not possible to rule out contribution of mouse VEGF to wound healing, as the growth factor peaked around the same time the microalgae died.

Whether HULK can achieve tissue regeneration in chronic wounds remains to be tested. Nevertheless, this study showed that incorporation of microalgae is a viable strategy to continuously supply oxygen to growing tissues, at least for body parts exposed to light.

M.. N. Chavez *et al*., Towards autotrophic tissue engineering: Photosynthetic gene therapy for regeneration. *Biomaterials* **75**, 25–36 (2016). [Abstract]