Oxygen Generating Gel for Tissue Salvage

Catherine L. Ward, Hung-Jen Wang, Anthony Atala, James J. Yoo, Benjamin S. Harrison
Wake Forest Institute for Regenerative Medicine, Wake Forest University Baptist Medical Center, Winston-Salem, NC, USA

Statement of Purpose: Most tissues in the body require an adequate source of oxygen and nutrients which are usually provided by an abundant and extensive blood supply. If tissue is removed from this supply, either by a blockage or trauma, ischemia quickly sets in and the tissue begins to enter an irreversible state of necrosis. Without immediate treatment to restore the oxygen supply, the tissue will begin to decompose. This can lead to loss of function and ultimately amputation. Muscle, a tissue in the body that requires a particular amount of oxygen for function, can be used as an example for this needed supplement. It is hypothesized that with a gel that can provide an oxygen additive, tissue ischemia, specifically muscle ischemia, can be prevented and the onset of necrosis can be delayed until a more permanent procedure for tissue restoration can take place.

Methods: Creation of an Oxygen-Generating Gel: An injectable gel was created for oxygen generation in a muscle model. Polyethylene glycol (PEG) was used as a vehicle with the incorporation of a chemical that generates oxygen in aqueous environments and an antioxidant. Optimization of an Oxygen-generating Gel: To test the capabilities of the oxygen-generating gel and to optimize it for the application of tissue salvage of muscle, the gel was evaluated in environments similar to native tissue. The water content and temperature of the muscle was mimicked in a synthetic environment. The gel was optimized to produce a specific amount of oxygen for the application of muscle salvage. *Ex vivo* Evaluation of Gel: The oxygen-generating gel was used in a preliminary study to determine if it had the ability to keep tissue in a viable state outside of the body. In this *ex vivo* model, the soleus muscle was removed from a mouse and placed in a solution at body temperature. Both oxygen-generating and control gels were injected into the muscles. The tissue, which would normally begin to degrade in this situation, incubated for several hours. At certain timepoints, the muscle was evaluated for sustained viability. *In vivo* Evaluation of Gel: With success in the *ex vivo* model, the gel was tested *in vivo*. This model consisted of tying off the femoral artery, vein and nerve in a mouse. The oxygen-generating and control gels were injected into the muscle. The mice were sacrificed at later timepoints to test the efficiency of the gel to keep the muscle viable without its main vasculature.

Results: Testing the oxygen generation of the gel provided a valid measurement of the capabilities of the gel in an environment similar to that of the muscle. This allowed changes to be made to the composition and makeup of the gel before any application experiments occurred. Alterations were made to benefit the state of ischemic muscle. In the *ex vivo* model, the oxygen generating materials established a source of oxygen to the ischemic tissue and was able to help maintain histomorphological characteristics similar to fresh native muscle (Figure 1). In the *in vivo* model, similar results were seen, as muscle injected with oxygen generating gels were able to act as native muscle, showing function even when the blood supply removed.

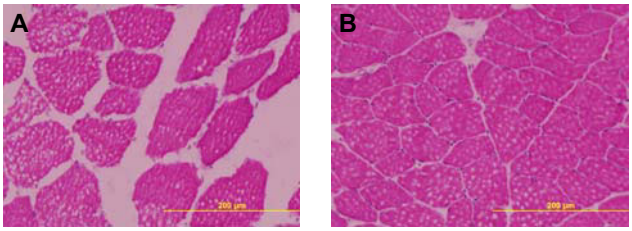

Figure 1. Histomorphological Results using Oxygen Generating Gels. Muscle was removed from the animal and incubated for 2 hours. A- Tissue injected with gel alone begins to show evident signs of ischemia: spacing between muscle filaments and fibers. B- Tissue injected with oxygen generating gels maintains native morphology.

Conclusions: An oxygen generating gel proved to provide a supplement to ischemic muscle tissue that maintained the histomorphological and functional characteristics of native tissue. This gel could possibly prolong the viability of tissue that has been cut off from a blood supply or removed from the body altogether, offering a way to buy time until more permanent measures can be taken to recover the tissue or organ. This applicable gel can be used on trauma wounds for a temporary burst of oxygen until a patient can reach appropriate medical treatment. It could also be used as a supplement for donor organs that need to be transported long distances before being implanted into a body. Future studies will analyze the extent of maintained function in the muscle with the supplemental gel and prolonging the length of oxygen production for an extended release.