Oxygen Generating Materials for Retaining Muscle Morphology and Function
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Introduction
Loss of functional skeletal muscle due to congenital and acquired conditions produces a physiological deficit for which there is still no effective clinical treatment. Tissue engineering of skeletal muscle in vitro for functional tissue replacement in vivo may provide a potential therapeutic solution to this unmet medical need. One major limiting factor to this approach is that skeletal muscle requires an adequate source of oxygen, one that is usually provided by a vascular network. However, in engineered tissue, this oxygen supply is not initially present. Particulate oxygen generators (POGs) may provide a solution. These particles have the ability to release oxygen when placed in aqueous environments, and have been shown to aid in providing oxygen in an ischemic skin flap model in mice.1 We hypothesized that a POG biomaterial could provide a supplemental source of oxygen for skeletal muscle in vitro which was capable of sustaining muscle morphology and maintaining function.

Materials and Methods
For in vitro cell culture testing, muscle precursor cells (MPCs) were isolated and grown in normoxic and hypoxic environments in the presence and absence of POGs. Cell morphology was analyzed using immnocytochemistry. For in vitro whole muscle function studies, rat extensor digitorum longus (EDL) muscle was isolated, sutured to a mounting post and force transducer, and evaluated in an organ bath at 37°C using electrical field stimulation (22V, 0.2 ms pulse). Muscles were injected with POGs dissolved in vehicle or with vehicle alone prior to an hour long contractile protocol consisting of three fatigue tests (100 Hz, 25 isometric contractions).

Results
In the presence of POGs, MPCs were able to both thrive and differentiate under hypoxic conditions, indicating that POG-derived supplemental oxygen was adequate for the cells (Figure 1). Preliminary EDL muscle functional results suggest that with the addition of POGs, skeletal muscle demonstrates an improved maintenance of function through the course of a prolonged fatiguing protocol (Figure 2).

Discussion and Conclusions
POGs appear to provide a critical supplemental oxygen source for myotube formation in culture as well as maintenance of whole muscle function in vitro. These initial results suggest that POGs may aid in engineering large tissue constructs by: 1) providing sufficient oxygen to promote muscle tissue formation in vitro, and 2) preserving engineered tissue viability and function in vivo until vascularization occurs.

References

Acknowledgments
This project is funded by NIH Grant AR05735.