Bioengineered Skeletal Muscle for Functional Defect Replacement in Muscle Injury Model

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Introduction
Loss of functional skeletal muscle due to congenital and acquired conditions, such as traumatic injury, tumor excision, etc., produces a physiological deficit for which there is still no effective clinical treatment. The goal of these studies is to develop clinically relevant skeletal muscle that can eventually be used for functional restoration of injured muscle in vivo. The rodent latissimus dorsi muscle (LD) model offers several advantages for this purpose in that it is a readily accessible, thin sheet of muscle with numerous existing clinical applications.

Materials and Methods
Tissue engineered skeletal muscle (TE-SKM) was developed by seeding rat myoblasts on Bladder Acellular Matrix (BAM) and preconditioned in a bioreactor. A model for the muscle injury was developed (Fig 1A) by excising ≈50% surface area of the LD muscle in a nu/nu mice and repaired by suturing TE-SKM constructs at the excised sites. Both the repaired LD (Fig 1B, C) and the contralateral native LD were explanted at either one month or two months after implantation. The maximal isometric contractile force was measured at optimal length with a 1200 ms train of 0.2 ms pulses, 20 V, 28 °C at different frequencies (1-150 Hz). Muscle caffeine contracture force was assessed using 50 mM caffeine at low-level electrical stimulation (0.2 Hz every 2 seconds) for the repaired and control groups.

Results

Functional Characterization of TE-SKM
Following implantation, TE-SKM constructs generated higher force than the non repaired group (12.6± 4.1 g) both at 1 month (16.88± 7.1 g) and 2 months (22.34±5.6g,p <0.05), the latter being ≈73% of that observed in native LD (30.67±4.4g). A similar trend was observed when contractile responses were expressed as specific force.

Analysis of Caffeine contracture force
LD repaired with bioengineered SKM constructs produced caffeine contracture force similar to contralateral control muscles two months after implantation. However, the peak isometric tetanic force produced by repaired LD muscles with TE-SKM constructs was still reduced by ~15%, compared to that of contralateral control LD suggesting that the reduction in force producing capacity of TE-SKM may be due to disruption of voltage-induced SR Ca\(^{2+}\) release.

Discussion and Conclusions
While further studies are clearly required, these initial observations indicate the applicability of this approach, specifically illustrating that following surgical removal of ≈50% of the LD muscle, implanted TE-SKM can recover ≈75% of the isometric tetanic force observed in native muscles within 2 months. In summary, the rodent LD defect model appears to be relevant for further proof of concept studies of the utility of TE-SKM.

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Disclosures
Authors have nothing to disclose.