Muscle Function Improvement in Injured Mice with Combination Treatment

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Introduction

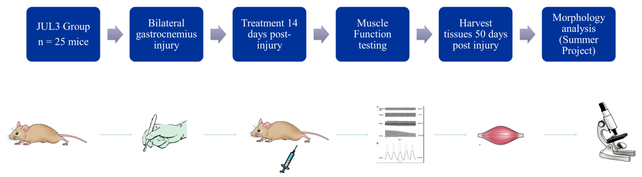
Loss of skeletal muscle from direct injury can present debilitating effects to an individual's quality of life and independence. Current treatments addressing muscle loss are limited by insufficient reconstitution of functional muscle. Novel regenerative medicine technologies include application of Urinary Bladder Matrix (UBM) and mesenchymal stem cells (MSCs) to restore functional muscle tissue. UBM is a porcine derived extracellular matrix serving as a scaffold for regeneration, aiming to restore function while decreasing scar tissue formation. In our previous studies, we found that UBM increased muscle myoblast cell proliferation. Therefore, we examined whether co-treatment with MSCs would further augment regeneration as compared to individual treatments.

Objective

To assess whether the UBM and MSC combination treatment is more effective as compared to individual treatments for achieving improvement in muscle function and morphology. We expect an improvement in muscle function, and an increase in both myofiber size and number using the combination treatment.

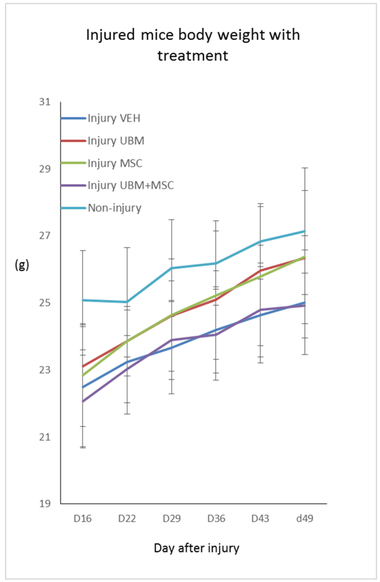
Experiment

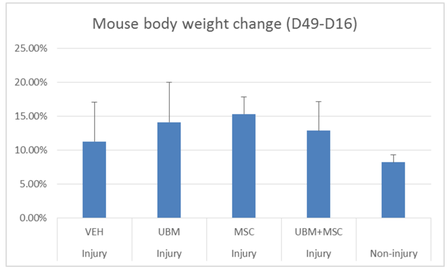
	Normal	Injury	Injury + UBM (150ug)	Injury + MCS(0.7 mil)	Injury + Combo
N	5	5	5	5	5

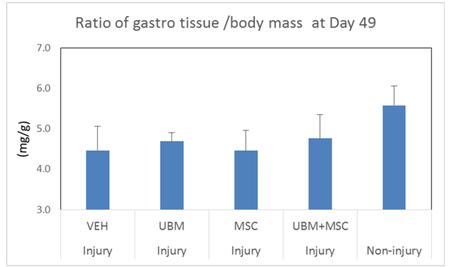


Results

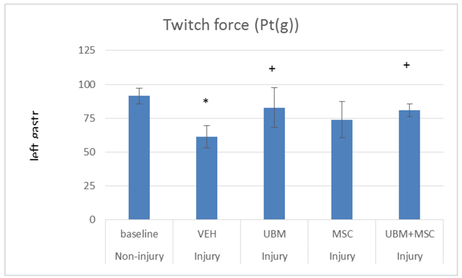
1. Body Mass and Tissue Weight

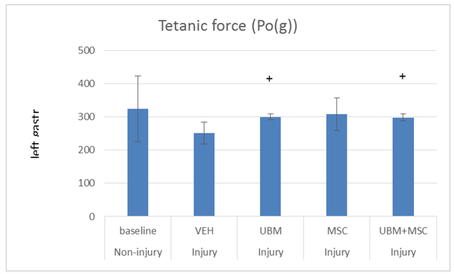




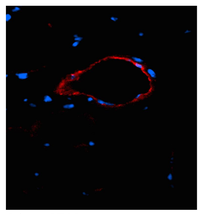


2. Muscle Isometric Force

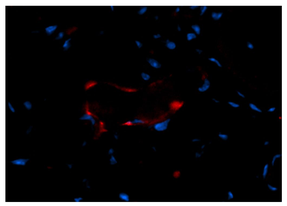




5. PECAM Immunofluorescence



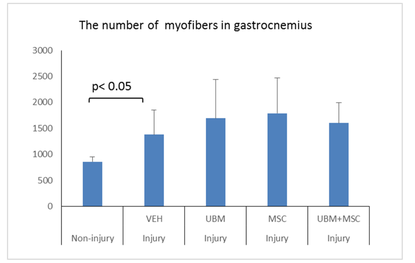
Injury + UBM

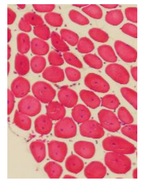


Injury + UBM/MSC

Images Above: PECAM Immunofluorescence (red),
DAPI counter stained nuclei (blue) muscle cross sectional plain (20X)

3. Myofiber Histology



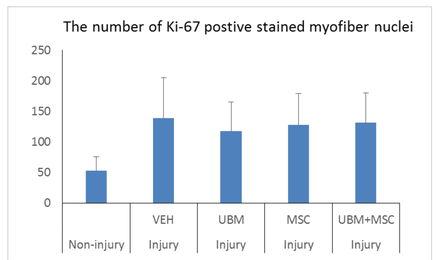


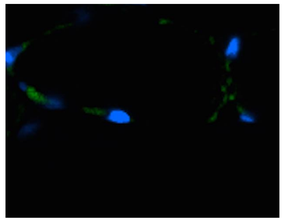
Injury + UBM

Injury + MSC

Images Above: H&E stained muscle cross sectional plain (20X) from injured mouse

4. Ki-67 Positive Stained Myofiber Nuclei





Injury + UBM/MSC

Image Above: KI-67 Immunofluorescence (green), DAPI counter stained (blue) muscle cross sectional plain (20X)

Summary

Muscle twitch (Pt) significantly decreased in the DMEM group compared to the non-injured group at day 50 ($p < 0.05$). Furthermore, twitch significantly increased with UBM treatment, but not with MSC treatment. Regenerating myofiber nuclei were counted and myofiber cross sectional area was measured with histology.
New myotubes were identified as having centrally located nuclei.
Ki-67 nuclear immunofluorescence staining was performed to demonstrate proliferating satellite cells. The myofiber cross sectional area and the number of Ki-67/DAPI overlapping stained nuclei significantly increased in the DMEM group compared to the non-injured group ($p < 0.05$). No differences were observed with other treatments in injured mice at day 49.

Acknowledgement

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References

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