3D Skeletal Muscle Modeling with Primary Human Cells
Applications in Metabolic Regulation and Muscle Atrophy

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Highlights

- Primary human skeletal muscle-derived cells (skMDCs) from Cook MyoSite enable integrated functional and metabolic profiling when cultured as 3D engineered muscle tissues (EMTs).
- EMTs exhibit insulin sensitivity and inducible atrophy, supporting human-relevant modeling for emerging clinical challenges such as GLP-1 receptor agonist-associated lean muscle loss.[1–3]

Generating Human Primary EMTs in Partnership with Cook MyoSite

Primary skeletal myoblasts robustly fuse into multinucleated myotubes, capture donor-dependent biological variability, and provide a physiologically relevant in vitro model of skeletal muscle function, metabolism, and disease.[4,5] To leverage these advantages, Curi Bio has identified Cook MyoSite's single-donor human skMDCs as our preferred primary cell source for 3D EMT studies. These cells readily integrate into Curi Bio workflows, are compatible with Curi Bio 3D media, and form EMTs with robust contractile function (**Figure 1A-D**), enabling scalable, physiologically relevant studies of skeletal muscle mechanisms, including metabolic regulation and atrophy.

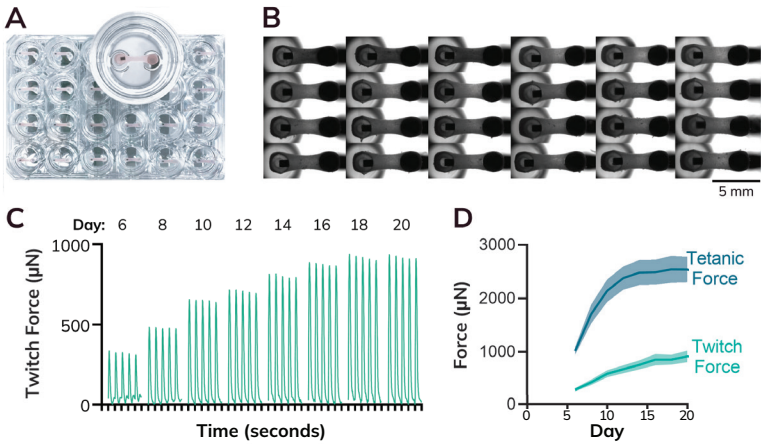


Figure 1. Cook MyoSite skMDC EMTs on the Mantarray platform exhibit robust contractile function. *(A) Schematic of the 24-well Mantarray EMT plate. (B) Representative image of Cook MyoSite skMDC-derived EMTs at day 20 of culture. (C) Averaged twitch responses to 1 Hz electrical pacing. (D) Quantified twitch and tetanic forces from days 6–20 of EMT culture (n = 3; mean ± SD).*

Quantitative Metabolic Assays in EMTs

The Mantarray platform enables quantitative metabolic interrogation of primary EMTs using complementary assays. First, glucose-starved EMTs loaded with 2-deoxy-D-glucose (2-DG) exhibited a clear insulin dose-response, with increasing 2-DG uptake at higher insulin concentrations (**Figure 2**).

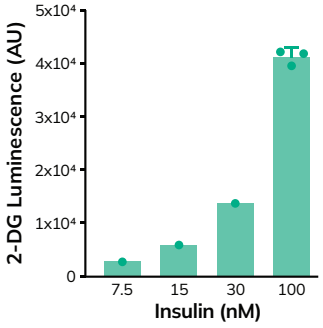


Figure 2. Insulin-dependent glucose uptake in primary human EMTs. *2-DG uptake following insulin stimulation (mean ± SD).*

Second, Mantarray™ enables concurrent metabolite measurements in EMTs and culture media, capturing physiologically expected glycogen and lactate responses to glucose starvation, insulin stimulation, exercise, and glucose reintroduction (**Figure 3**). Together, these results demonstrate that Mantarray-cultured EMTs support stimulus-dependent regulation of glucose uptake, glycogen storage, and glycolytic output, enabling integrated functional and metabolic analyses within a single platform.[5]

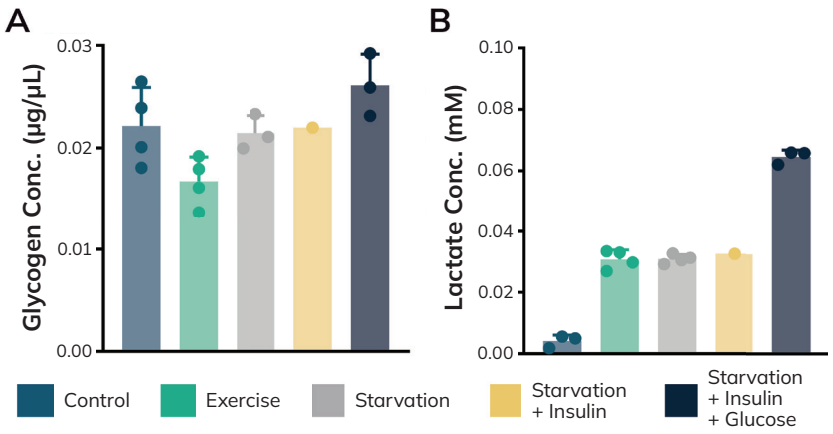


Figure 3. Metabolite profiling in EMTs. *(A) Intracellular glycogen and (B) secreted lactate are modulated by exercise, glucose availability, and insulin (mean ± SD).*

Modeling Skeletal Muscle Atrophy

Skeletal muscle atrophy was modeled by activating TGF-*β*/activin A signaling in Cook MyoSite skMDC-derived EMTs, where activin A induced progressive functional decline in twitch force (**Figure 4**).[6] Consistent with known anabolic effects, antibody-based blockade of ActRIIA/IIB signaling prevented activin A-induced functional deficits measured on the Mantarray platform.

Conclusion

Curi Bio's ecosystem for 3D EMTs enables parallel functional and biochemical measurements, providing a physiologically relevant system for modeling insulin sensitivity, metabolism, and muscle atrophy to support drug discovery while de-risking treatment-induced sarcopenia. The use of Cook MyoSite single-donor human skMDCs further strengthens this approach by providing a robust, human-relevant primary cell source that integrates seamlessly into scalable 3D EMT workflows.

Curious how Curi Bio can advance your skeletal muscle metabolism and atrophy research? Our scientists are ready to partner with you to generate decision-driven human functional data using Curi Bio platforms and research services. Contact us at sales@curibio.com.

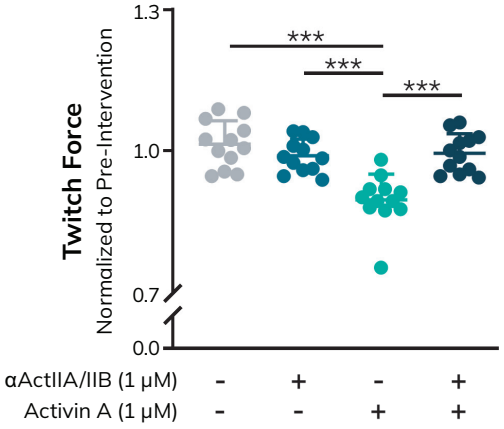


Figure 4. TGF-β/activin A signaling modulates atrophy-associated loss of contractile function. *Antibody-based blockade of activin signaling preserves twitch force in primary EMTs (mean ± SD; adapted from Carlsson et al., 2025; CC BY 4.0).*

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References

[1] Wilding *et al.*, **N Eng J Med**, 2021; [2] Neeland *et al.*, **Diabetes Obes Metab**, 2024; [3] Linge *et al.*, **Circulation**, 2024; [4] Francis *et al.*, **J Muscle Res Cell Motil**, 2025; [5] Henriquez-Olguin *et al.*, **bioRxiv**, 2026; [6] Carlsson *et al.*, **bioRxiv**, 2025;