SELF-ORGANIZATION AND CONTRACTILITY OF SKELETAL AND CARDIAC MUSCLE TISSUE IN CULTURE

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Both skeletal and cardiac myocytes from mammals can be readily induced to self organize into small cylindrical tissue constructs in vitro, without the need for scaffold materials in the contractile region of the tissue construct. The constructs, termed "myooids" in the case of skeletal muscle, and "cardioids" in the case of cardiac muscle, are typically 10-12 mm in length, and range from 40 to 500 microns in diameter, depending upon many factors including the source of the cells, the plating density, substrate surface adhesion, and growth media constituents. The process of tissue self-organization is mediated by the gradual release of a cohesive monolayer of spontaneously contracting cells from a prepared substrate material, while maintaining cell adhesion to two anchor materials, spaced ~ 1 cm apart.. The constructs can generally be maintained in culture for periods longer than one month, and in some cases up to ~5 months, during which time they spontaneously contract and are electrically excitable. Tendon-like structures are provided at each end, constructed of laminin-coated braided silk suture, so that the tissues may be readily attached to servo motors and force transducers for functional assessments. In the absence of externally-applied stimuli, the contractility of these aneural and avascular constructs remains low (~1 to 10% of control adult values), indicating incomplete tissue development in vitro. The protocol for culturing and functionally evaluating self-organized muscle tissues is general, and with minor modifications will work for cell lines or primary cells from any skeletal muscle yet tested from neonatal, adult, or aged mammals, including rats, mice, cows, and pigs.