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Membrane fusion in muscle development and repair

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Abstract
Mature skeletal muscle forms from the fusion of skeletal muscle precursor cells, myoblasts. Myoblasts fuse to other myoblasts to generate multinucleate myotubes during myogenesis, and myoblasts also fuse to other myotubes during muscle growth and repair. Proteins within myoblasts and myotubes regulate complex processes such as elongation, migration, cell adherence, cytoskeletal reorganization, membrane coalescence, and ultimately fusion. Recent studies have identified cell surface proteins, intracellular proteins, and extracellular signaling molecules required for the proper fusion of muscle. Many proteins that actively participate in myoblast fusion also coordinate membrane repair. Here we will review mammalian membrane fusion with specific attention to proteins that mediate myoblast fusion and muscle repair.

Keywords
Fusion, Repair, Membrane, Myoblast, Muscle, Development

Abberviation
CK Creatine Kinase, DMD Duchenne Muscular Dystrophy, EHD Eps15 Homology Domain, FC Founder Cell, FCM Fusion Competent Myoblasts, LGMD limb girdle muscular dystrophy, PH pleckstrin homology, PIP2 Phosphatidylinositol 4,5-bisphosphate, PS phosphatidyl serine, T-tubule transverse tubule

1. Introduction

Striated muscle is characterized by a highly ordered intracellular array of sarcomeres optimized for contraction (Figure 1). The sarcolemma protects myofibers and is contiguous with the Transverse (T)-tubules, a network responsible for coordinating excitation and contraction by tightly regulating Ca^{2+} release into the myoplasm [1]. Ca^{2+} channels and exchangers reside in the T-tubules, and the T-tubules are flanked by the sarcoplasmic reticulum (SR), a reservoir for the majority of intracellular Ca^{2+}. Protein complexes enriched in the sarcolemma are specialized for attachment to the surrounding matrix, and include the integrins and dystrophin glycoprotein complex (DGC) [2]. The stem cells of muscle, the satellite cells, are located between the sarcolemma and the basal lamina. Upon muscle injury, this regenerative cell population divides and differentiates into myoblasts, which then fuse to regenerate the muscle [3]. Herein, we review membrane fusion events in myoblast fusion, in development and repair.