ENCONTROS SCIENTIA

How muscle stem cells are maintained during epaxial myogenesis? An evolutionary perspective

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Myogenesis, the process of generating skeletal muscle, is a complex event that starts during embryonic development and extends throughout adulthood. Understanding the mechanisms underlying skeletal muscle development can provide cues about how skeletal muscle evolved, from ancestral swimming vertebrates to terrestrial amniotes with a variety of locomotory capacities. Skeletal muscle first arises in the embryonic myotomes, transient axial segmented units that in developing amniote embryos are progressively transformed into the complex epaxial (deep back) and hypaxial (intercostal and body wall) musculature. The construction of functional skeletal muscle tissue during development involves a specific set of genetically established myogenic stages. First, certain gene expression patterns assure the commitment of the myogenic precursor cells (MPCs) to the myogenic lineage, which occurs prior to myotome formation. Then some of these cells are specified to enter the myogenic program and undergo terminal differentiation and originate the primordia of the distinct muscle masses. Interestingly, MPCs form a heterogenous population characterized by different behaviors. When these populations colonize the myotome, some differentiate and form skeletal muscle, while others remain proliferative, contributing to form a resident pool of muscle stem cells, that contribute to muscle growth and will be crucial for muscle regeneration and health after birth. Do the characteristics of distinct MPC populations impact the spatial organization of myogenic progenitor and differentiated cells into the correct positioning of muscle groups? Is the myotome important for the organization and viability of MPCs during skeletal muscle morphogenesis? These are the some of the main questions that our team is trying to address.

To do so, we use a double knockout mouse line, where mutant embryos do not form the myotome but skeletal muscles still form. Our analysis revealed that these embryos lack specific epaxial (deep back) muscles, while other muscles seem to form normally. The absence of these epaxial muscle groups can be explained by a deficient myogenic differentiation program, due to the inefficiency of maintaining a specific population of muscle stem cells. More importantly, we found that in wild-type embryos, a specific signaling pathway, initiated by the differentiated cells in the myotome, is crucial to maintain the myogenic identity of this particular population of MPCs and may therefore be vital for the formation of a subset of the epaxial muscles in mutant embryos. Together, our data points to the existence of two different epaxial myogenic differentiation programs that may be evolutionary distinct but operate synchronously during epaxial muscle morphogenesis in amniotes.

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FCUL (Building C2), 12h00-13h00, room 2.2.14

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