Logics and properties of a genetic regulatory program that drives embryonic muscle development in an echinoderm

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Abstract Evolutionary origin of muscle is a central question when discussing mesoderm evolution. Developmental mechanisms underlying somatic muscle development have mostly been studied in vertebrates and fly where multiple signals and hierarchic genetic regulatory cascades selectively specify myoblasts from a pool of naive mesodermal progenitors. However, due to the increased organismic complexity and distant phylogenetic position of the two systems, a general mechanistic understanding of myogenesis is still lacking. In this study, we propose a gene regulatory network (GRN) model that promotes myogenesis in the sea urchin embryo, an early branching deuterostome. A fibroblast growth factor signaling and four Forkhead transcription factors consist the central part of our model and appear to orchestrate the myogenic process. The topological properties of the network reveal dense gene interwiring and a multilevel transcriptional regulation of conserved and novel myogenic genes. Finally, the comparison of the myogenic network architecture among different animal groups highlights the evolutionary plasticity of developmental GRNs.

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Introduction

Muscle cells are present in most animals with the characteristic of containing protein filaments that slide and produce contractions. In bilaterians, muscles develop usually from mesodermal cells in a process called myogenesis, during which the naive mesodermal progenitors are selectively specified as myoblasts and later differentiate into muscle cells. In vertebrate embryos, the mesoderm is subdivided into several regions from which different muscle types originated. For example, the axial skeletal muscles originate in the segmented paraxial mesoderm called somites, whereas the cardiac muscles develop from the lateral plate mesoderm. The subdivisions of different mesoderm regions require differential expression of the Forkhead (Fox) family of transcription factors, such as FoxC1 and FoxC2 for the paraxial mesoderm (Wilm et al., 2004) and FoxF1 for the lateral plate mesoderm (Mahlapuu et al., 2001). Analyses of molecular mechanisms underlying myogenesis in various parts of the somites further lead to a series of complex gene regulatory networks (GRNs) (Bryson-Richardson and Currie, 2008; Yokoyama and Asahara, 2011; Bentzinger et al., 2012). These networks are composed of multiple signals that drive the expression of the genes encoding basic helix-loop-helix (bHLH) domain-containing myogenic regulatory factors, which include myogenic differentiation 1 (MyoD), myogenic factor 5 (Myf5), Myf6, and myogenin (Myog). Other factors, including the myocyte enhancer binding factor 2 (MEF2) family of MADS-box proteins, transcription factors Pitx2, Pitx3, sine oculis-related homeobox (six) family members and their cofactors eyes-absent homologs (Eya), are also involved in specification and migration of the myogenic precursor cells (Molkentin and Olson, 1996; Yokoyama and Asahara, 2011). These myogenic transcriptional regulators then in turn initiate the transcription of muscle differentiation markers, such as myosin heavy chain proteins (MHC), that determine the morphological