Seminars in Cell & Developmental Biology 72 (2017) 56–66

Contents lists available at ScienceDirect

Seminars in Cell & Developmental Biology

journal homepage: www.elsevier.com/locate/semcdb

Review

Drosophila adult muscle development and regeneration

Rajesh D. Gunage[a,b], Nagaraju Dhanyasi[a,c], Heinrich Reichert[d], K. VijayRaghavan[a,*]

[a] National Centre for Biological Sciences, Tata Institute of Fundamental Research, India
[b] Stem Cell Program and Division of Hematology/Oncology, Children's Hospital Boston, Howard Hughes Medical Institute, Boston, MA 02115, United States
[c] Department of Molecular and Cellular Biology, Center for Brain Science, Harvard University, Cambridge, MA 02138, United States
[d] Biozentrum, University of Basel, Basel, Switzerland

ARTICLE INFO

Article history:
Received 23 October 2017
Received in revised form 8 November 2017
Accepted 11 November 2017
Available online 16 November 2017

Keywords:
Muscle stem cell
Myogenesis
Myoblasts
Niche
Epithelial tissue
stripe
Myoblast fusion
Satellite cell
Zfh-1

ABSTRACT

Myogenesis is a highly orchestrated, complex developmental process by which cell lineages that are mesodermal in origin generate differentiated multinucleate muscle cells as a final product. Considerable insight into the process of myogenesis has been obtained for the embryonic development of the larval muscles of *Drosophila*. More recently, the postembryonic development of the muscles of the adult fly has become a focus of experimental investigation of myogenesis since specific flight muscles of the fly manifest remarkable similarities to vertebrate muscles in their development and organization. In this review, we catalog some of the milestones in the study of myogenesis in the large adult-specific flight muscles of *Drosophila*. The identification of mesoderm-derived muscle stem cell lineages, the characterization of the symmetric and asymmetric divisions through which they produce adult-specific myoblasts, the multifaceted processes of myoblast fusion, and the unexpected discovery of quiescent satellite cells that can be activated by injury are discussed. Moreover, the finding that all of these processes incorporate a plethora of signaling interactions with other myogenic cells and with niche-like neighboring tissue is considered. Finally, we briefly point out possible future developments in the area of *Drosophila* myogenesis that may lead to of new avenues of genetic research into the roles of muscle stem cells in development, disease and aging.

Contents

1. Introduction

The muscles of metazoans power a wide range of movements such as walking, running, climbing, and flying and, although there is considerable variation, they generally make the largest contribution to the body mass of most animals [1,2]. In developmental

* Corresponding author.
E-mail address: vijay@ncbs.res.in (K. VijayRaghavan).

https://doi.org/10.1016/j.semcdb.2017.11.017

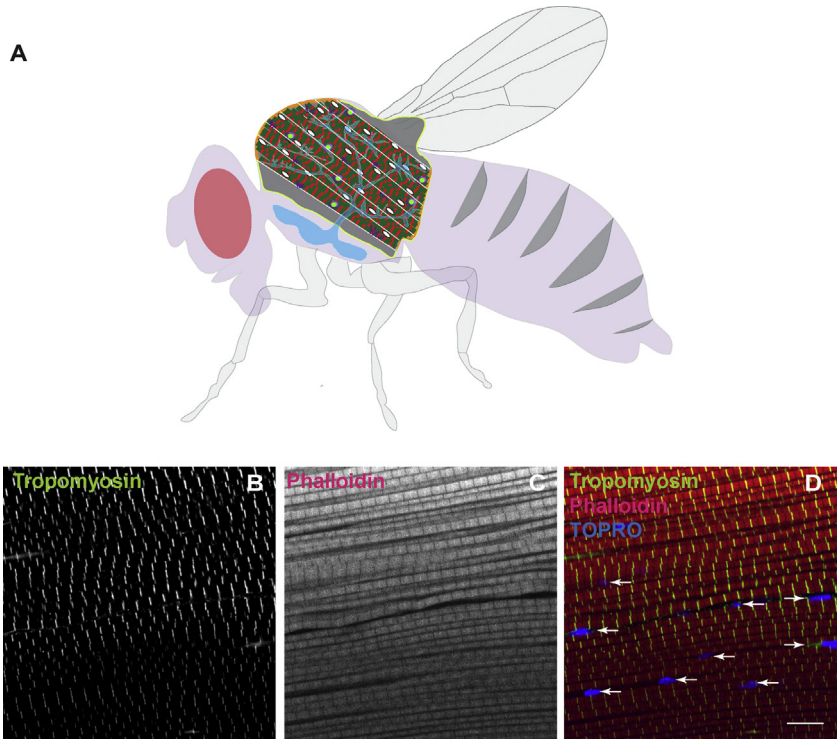

Fig. 1. A) Schematic showing adult fly thorax with six dorsal lateral muscles innervated by motor neuron (Blue). B–D) Optical section of flight muscles stained for Tropomyosin-GFP (anti-GFP, Green), phalloidin (marks F-actin, Red) and TOPRO-3 (Blue, marks all nuclei). Arrows shows position of the nuclei in the muscle syncytium.

terms, muscles derive from the mesoderm, a germ layer that together with the ectoderm and endoderm give rise to the various tissues and organs that make up the bilaterian body. In cellular terms, and contrasting with most other cell types, mature muscle cells are generally characterized by the presence of numerous nuclei. How this multinucleate syncytial organization of muscle cells originates from mononucleate precursor cells of mesodermal origin (often generically referred to as "myoblasts") during early development is a major question in muscle biology.

To address this question, developmental biologists have turned to a number of vertebrate and invertebrate model systems. Investigations carried out on one of these model systems, the fruit fly *Drosophila melanogaster*, have been useful to understanding many aspects of organismal development, especially as concerns the early stages of development, and have led to the identification and characterization of numerous conserved developmental control genes that operate in animal embryogenesis. Work focused on the development of the *Drosophila* mesoderm and its derivatives, notably the somatic, cardiac and visceral muscles, has resulted in remarkable insight into the genetic mechanisms of myogenesis. Moreover together with comparative studies on the development of vertebrate skeletal muscle, this work has uncovered conserved molecular pathways for myogenesis and identified similar cellular processes involved in transforming mononucleate myoblastic precursors into mature multinucleate muscle cells [2–4].

The indirect flight muscles (IFMs) have many developmental characteristics similar to that of vertebrate muscle. The IFMs consist of two groups of large muscles, the dorsoventral muscles (DVMs) and the dorsal longitudinal muscles (DLMs), which together power the wing stroke during flight (Fig. 1). We focus on the DLMs for much of this report. Like vertebrate muscle cells, the multifiber IFMs are formed during development by the fusion of muscle stem cell-derived myoblasts with a set of developing fibres and, once mature, manifest 'fibrillar' organization in contrast to the tubular organization of other fly muscles [5]. Many shared features of IFMs and vertebrate somatic muscle cells have made these *Drosophila* muscles excellent models for developmental genetic investigations of key aspects of myogenesis [6–10].

In this review, we consider recent findings on the cellular and molecular mechanisms involved in the development of one group of IFMs, the DLMs focusing on mesoderm-derived muscle stem cell lineages, the symmetric and asymmetric divisions through which they produce myoblasts, the multifaceted processes of myoblast fusion with template cells, and the recently discovered muscle satellite cells. In doing so, we embark on a journey from their mesodermal origins along a developmental timeline that incorporates a plethora of signaling interactions with other myogenic cells and with niche-like neighboring tissue to the ultimate formation of mature muscle cells and of quiescent satellite cells, which can be activated by injury. Finally, we will briefly point out possible future developments in the area of *Drosophila* myogenesis.

2. Myogenic beginnings: from mesoderm to muscle progenitors

Somatic myogenesis in *Drosophila* is a two-stage process. The muscles of the larval stage are generated during embryogenesis and are largely destroyed during pupal stages at metamorphosis. By contrast, the muscles of the adult are generated de novo during the postembryonic larval and pupal stages. Remarkably, however, the cells of the adult musculature are related to cells of the embryonically generated larval muscles as members in a common lineage that can be traced back to specified progenitor cells that arise in specific domains of the embryonic mesoderm [11].

Formation of the mesoderm begins during early embryogenesis through the process of gastrulation in which cells located ventrally, that express high nuclear levels of the maternally provided Dorsal protein, invaginate into the embryo along a ventral furrow [12]. This initial specification of mesodermal cells requires the activation by Dorsal of two zygotic genes that encode the basic helix-loop-helix transcription factor Twist, a key regulator of mesodermal tissue formation, and the transcription factor Snail. The Twist/Snail positive