Biochemistry and Biophysics Reports 6 (2016) 209–219

Contents lists available at ScienceDirect

Biochemistry and Biophysics Reports

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

The epigenetic regulation of embryonic myogenesis and adult muscle regeneration by histone methylation modification

Wei Jin [a], Jian Peng [b,1], Siwen Jiang [a,c,*,1]

[a] Key Laboratory of Pig Genetics and Breeding of Ministry of Agriculture & Key Laboratory of Agricultural Animal Genetics, Breeding and Reproduction of Ministry of Education, Huazhong Agricultural University, Wuhan 430070, PR China
[b] Department of Animal Nutrition and Feed Science, College of Animal Science and Technology, Huazhong Agricultural University, Wuhan 430070, Hubei, PR China
[c] Key Projects in the Cooperative Innovation Center for Sustainable Pig Production of Wuhan, PR China

ARTICLE INFO

Article history:
Received 29 December 2015
Received in revised form
14 April 2016
Accepted 18 April 2016
Available online 20 April 2016

Keywords:
Myogenesis
Muscle progenitor cells
Muscle differentiation
Muscle regeneration
Epigenetic
Histone methylation/demethylation modification

ABSTRACT

Skeletal muscle formation in vertebrates is derived from the paraxial mesoderm, which develops into myogenic precursor cells and finally differentiates into mature myofibers. This myogenic program involves temporal-spatial molecular events performed by transcription regulators (such as members of the Pax, MRFs and Six families) and signaling pathways (such as Wnts, BMP and Shh signaling). Epigenetic regulation, including histone post-translational modifications is crucial for controlling gene expression through recruitment of various chromatin-modifying enzymes that alter chromatin dynamics during myogenesis. The chromatin modifying enzymes are also recruited at regions of muscle gene regulation, coordinating transcription regulators to influence gene expression. In particular, the reversible methylation status of histone N-terminal tails provides the important regulatory mechanisms in either activation or repression of muscle genes. In this report, we review the recent literatures to deduce mechanisms underlying the epigenetic regulation of gene expression with a focus on histone methylation modification during embryo myogenesis and adult muscle regeneration. Recent results from different histone methylation/demethylation modifications have increased our understanding about the highly intricate layers of epigenetic regulations involved in myogenesis and cross-talk of histone enzymes with the muscle-specific transcriptional machinery.

Contents

Abbreviations: SCs, satellite cells; MRFs, myogenic regulatory factors; bHLH, basic helix-loop-helix; MEF2, myocyte enhancer factor 2; Shh, sonic hedgehog; BMP4, bone morphogenic protein 4; p38 MAPK, p38 mitogen-activated protein kinase; H3K4, methylation of histone H3 lysine 4; H3K9, methylation of histone H3 lysine 9; H3K27, methylation of histone H3 lysine 27; PRC2, polycomb repressive complex 2; LSD1, lysine specific demethyltransferase 1; KDMs, lysine demethyltransferases; UTX, ubiquitously transcribed tetratricopeptide repeat, X chromosome; ChIP, chromatin immunoprecipitation; TSS, transcription start sites

* Correspondence to: College of Animal Science and Technology, Huazhong Agricultural University, Wuhan 430070, PR China.
E-mail address: jiangsiwen@mail.hzau.edu.cn (S. Jiang).
[1] Contributed equally to this work.

http://dx.doi.org/10.1016/j.bbrep.2016.04.009

1. Introduction

Embryo myogenesis or adult muscle regeneration is the programming of a population of muscle progenitors, embryonic or fetal myoblasts and satellite cells (SCs) into committing to the myogenic lineages and of myoblasts into differentiating into mature myofibers. The formation of skeletal muscles involves both genetic and epigenetic changes that culminate in alterations in gene expression [1]. Chromatin-modifying enzymes and remodeling complexes orchestrate the pattern of gene expression and reprogram the myogenic lineage toward terminal differentiation [1,2]. The transcriptional regulation of muscle specification has been well characterized, and the role of histone acetylation modification in control of muscle-specific gene expression has been studied extensively, however, less is known about the role of histone methylation modification in this process [3]. Here, we review the potential roles of histone modifications during myogenesis with a focus on H3 lysine 27 tri-methylation ($H3K27me^3$), H3 lysine 4 tri-methylation ($H3K4me^3$) and H3 lysine 9 di/tri-methylation ($H3K9me^{2/3}$) markers at myogenic gene regulatory regions in myoblasts and satellite cells.

2. Myogenesis: gene regulatory networks and transcriptional mechanisms

2.1. Development of embryo myogenesis

Skeletal muscle is initiated in the somite (epithelial spheres along the anterior–posterior axis of the embryo) which derives from paraxial mesoderm adjacent to the neural tube and notochord [2,4,5]. The newly formed dorsal somites rapidly differentiate into dermomyotomes, which are the source of muscle precursor cells. Cells from the dorsomedial part of the somites adjacent to the neural tubes migrate under the dermomyotomes to form the myotomes [6]. The myotomes are committed and differentiate into myoblasts, and final maturation of myotubes fuse into myofibers (Fig. 1). The epaxial (dorso-medial) part of the dermomyotomes and myotomes generate the back muscles while the hypaxial (ventro-lateral) somites generate the rest of the trunk and limb muscles [7–9].

2.2. Genetic regulatory networks in myogenesis

2.2.1. Regulation of transcription regulators in myogenesis

The paired-homeobox family of transcription factors Pax3 and Pax7 are important upstream regulators of the myogenic process in the embryo myogenesis. In Splotch mice, because of mutation of *Pax3*, cells fail to develop the hypaxial domain of the somite and thus lack limb musculature and other muscle masses in the body. However, epaxial-derived muscles are less affected [6,10–12]. In the chick embryo, *Pax3*:*Pax7*-positive cells are maintained as proliferating cells and do not express myogenic regulatory factors or muscle proteins. However, they can give rise to skeletal muscle cells leading to subsequent skeletal muscle differentiation and producing muscle satellite cells [13]. *Pax3*:*Pax7* double mutants die at early fetal stages. In the absence of both Pax3 and Pax7 proteins, muscle progenitor cells do not activate the myogenic determination genes to enter the myogenic program [14].

The myogenic regulatory factors (MRFs) of *MyoD*, *Myf5*, *myogenin* and *Mrf4* genes have highly conserved basic helix-loop-helix domain (bHLH) structure and are expressed in the skeletal muscle

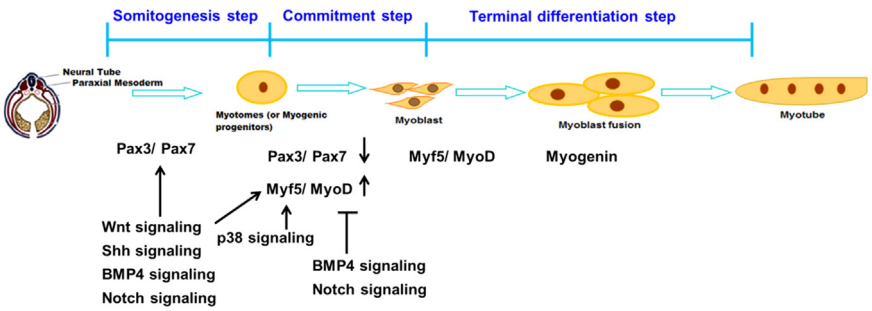

Fig. 1. A schematic representation of developmental myogenesis. It shows that the somites give rise to muscle progenitor cells, progenitor cells determinate and proliferate as myoblasts, and myoblasts differentiate into myotubes. During this process, the action of both positive and negative signals control the spatio-temporal expression of muscle genes. And gene regulatory networks are performed by myogenic transcriptional factors.