Biochimica et Biophysica Acta 1849 (2015) 626–636

Contents lists available at ScienceDirect

Biochimica et Biophysica Acta

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

Review

Establishing pluripotency in early development

Sarita S. Paranjpe, Gert Jan C. Veenstra *

Radboud University, Department of Molecular Developmental Biology, Faculty of Science, Radboud Institute for Molecular Life Sciences, Nijmegen, The Netherlands

ARTICLE INFO

Article history:
Received 12 January 2015
Received in revised form 26 March 2015
Accepted 30 March 2015
Available online 7 April 2015

Keywords:
Pluripotency
Embryo
Chromatin
Methylation
Zygotic genome activation

ABSTRACT

The earliest steps of embryonic development involve important changes in chromatin and transcription factor networks, which are orchestrated to establish pluripotent cells that will form the embryo. DNA methylation, histone modifications, the pluripotency regulatory network of transcription factors, maternal factors and newly translated proteins all contribute to these transitions in dynamic ways. Moreover, these dynamics are linked to the onset of zygotic transcription. We will review recent progress in our understanding of chromatin state and regulation of gene expression in the context of embryonic development in vertebrates, in particular mouse, *Xenopus* and zebrafish. We include work on mouse embryonic stem cells and highlight work that illustrates how early embryonic dynamics establish gene regulatory networks and the state of pluripotency.

© 2015 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction: routing fertilized eggs to pluripotency

At the very beginning of embryonic development two specialized and highly differentiated cells, the gametes, fuse to form the zygote which in turn produces all cell types of the organism (as well as extra-embryonic tissue in the case of mammals, see below). The parental genomes show different histone modification patterns and are subject to dramatic chromatin reorganization, DNA demethylation and remethylation after fertilization and during early development, in order to reprogram the sperm and oocyte epigenomes [1–7]. Early in development a maternal to zygotic transition (MZT) is triggered, which passes regulatory control of development from maternal to newly synthesized components [8,9]; this regulatory event can be defined as the period of time encompassing the initial degradation of maternal transcripts, zygotic genome activation (ZGA, the onset of transcription), until the first major morphological requirement for zygotic transcripts in embryonic development [9]. Following the ZGA, pluripotent cells emerge which will give rise to the three germ layers of the embryo, ectoderm, mesoderm and endoderm, however the relationship between ZGA and pluripotency is different between mammals and non-mammalian vertebrates (Fig. 1, Table 1).

In amniotic species such as mammals, the zygote starts transcribing its own genes just before the two-cell stage. Subsequently, trophectoderm and primitive endoderm, cell lineages that contribute to placental development, are set up in addition to the pluripotent cells of the inner cell mass of the blastocyst that will form the organism (Fig. 1). Therefore the mammalian zygote is referred to as totipotent, being able to produce all cell types of both the embryo proper and embryonic placental tissues [10].

Although early embryonic development is strikingly different in *Xenopus* and zebrafish compared to mouse, pluripotency and subsequent germ layer commitment, patterning and convergent extension are functionally highly analogous in these species. In *Xenopus* and zebrafish early cleavage development produces a blastula embryo, which undergoes ZGA (Fig. 1). This is also referred to as the mid-blastula transition (MBT) [8,9,11]. Cell cycle lengthening and the acquisition of cell motility coincide with the onset of embryonic transcription at the MBT [11] and at this stage, at and immediately after the MBT, cells at the animal pole of the embryo are pluripotent (Fig. 1). These cells are normally fated to give rise to ectoderm (epidermal ectoderm and neural ectoderm) but can also give rise to mesoderm and endoderm derivatives when exposed to specific factors [12].

Pluripotency, as it emerges from the zygote, represents a functional cellular state, much in the same way differentiated cells have a defined set of biochemical and cellular properties. These properties emerge from a cell type-specific reading of the genomic sequence information, which is part of what is referred to as epigenetic regulation. At the molecular level this involves chemical modifications of either the DNA itself (for example methylation of cytosine residues) or the chromosomal proteins associated with genomic DNA (chromatin). The profiles of epigenetic modifications can vary between cells and developmental stages and form a molecular regulatory intermediate between genomic sequence information and biochemical and cellular properties of cells. Epigenetics therefore constitutes a developmental stage- and cell type-specific filter of genomic sequence information.

In this review we compare vertebrate studies on the pluripotent chromatin state and how it emerges during embryonic development.

* Corresponding author.
E-mail address: g.veenstra@science.ru.nl (G.J.C. Veenstra).

http://dx.doi.org/10.1016/j.bbagrm.2015.03.006
1874-9399/© 2015 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

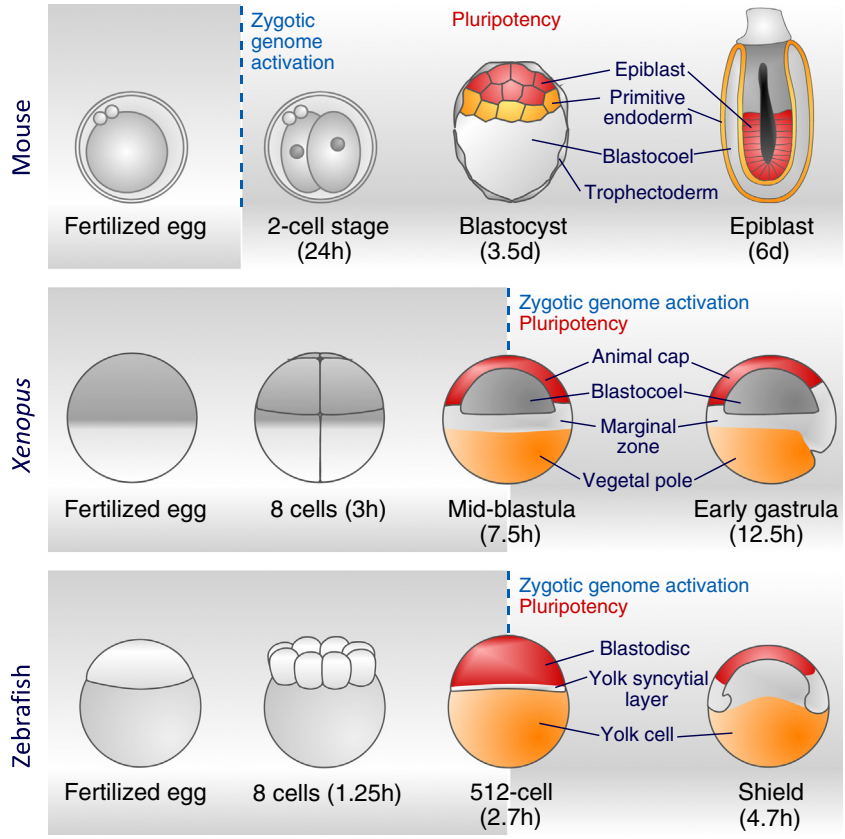

Fig. 1. Embryonic development in relation to zygotic gene activation (ZGA) and pluripotency in mouse (top panel), *Xenopus* (middle panel) and zebrafish (bottom panel). ZGA occurs at the late 1-cell stage in mouse, but does not happen until the 12th and 10th cell cycle in *Xenopus* and zebrafish respectively. In mouse, before pluripotency is established two other lineages, trophectoderm and primitive endoderm, need to be formed. The inner cell mass (ICM) epiblast cells of the pre-implantation blastocyst (mouse, 3.5 days, red cells) represent the ground state of pluripotency in vivo, whereas in day 6 embryos (still before gastrulation) these cells have been primed towards differentiation. In *Xenopus*, vegetal pole cells have been maternally specified to form endoderm and secrete signals to induce mesoderm in the marginal zone. Animal pole cells (red) correspond to the pluripotent cells of the mid-blastula embryo. Times post-fertilization are indicated for *X. laevis* at 22 °C. In zebrafish, the mid-blastula transition (MBT) starts two cell cycles earlier. Zebrafish has one large yolk cell which does not divide. The nuclei from blastodisc cells closest to the yolk cell form a syncytium with the yolk cell. This region has a mesendodermal fate. Zebrafish times post-fertilization are temperature-dependent and indicated at 28.5 °C.

We will discuss DNA methylation, histone modifications, *cis*-regulatory elements and transcription factors that prime the zygote for pluripotency. We will illustrate the findings from mouse, frog and fish embryo models but also discuss findings in cellular models of pluripotency such as mouse embryonic stem (ES) cells where warranted. ES cells represent stable pluripotency in vitro, whereas embryonic pluripotency is transitory. However much has been learned from these systems that also is highly relevant for pluripotency in vivo. The reader is referred to excellent reviews for other aspects of pluripotent chromatin and embryogenesis, including more detailed discussions of the MZT [8,9], chromatin interactions and complexes [13–17], and naive and primed pluripotency in cell culture [18,19].

2. Global DNA methylation dynamics in relation to pluripotency

2.1. DNA methylation dynamics in mammalian development

DNA methylation is an important epigenetic modification with a role in a variety of processes, including tissue-specific gene expression, development and cellular differentiation, carcinogenesis and aging, and specifically for mammals, genomic imprinting and X chromosome inactivation [20–22]. Methylation at the 5-position of cytosine (5mC) occurs mainly at CG dinucleotides (commonly referred to as CpG dinucleotides) in vertebrates and is a prerequisite for normal embryogenesis; the DNA methyltransferases DNMT1, DNMT3a and DNMT3b are all essential for early mouse development [23,24]. DNA methylation

Table 1
Overview of early development and pluripotency in mouse, *Xenopus* and zebrafish. Note the interspecific differences in the relationship between (1) zygotic genome activation (ZGA) and pluripotency and (2) DNA methylation and pluripotency. Abbreviations: hypoM, hypomethylated; hyperM, hypermethylated; deM, demethylated; ND, not determined.

	Mouse	*Xenopus*	Zebrafish
ZGA stage	2 cells	Blastula	512 cells
Pluripotent stage	Blastocyst (E3.5)	Blastula	512 cells
Global DNA methylation	hypoM at ZGA and pluripotency	hyperM at ZGA and pluripotency	hyperM at ZGA and pluripotency
Paternal DNA methylation	hyperM, active deM after fertilization	ND	hyperM, maintained
Maternal DNA methylation	Relatively hypoM, passive deM	ND	Relatively hypoM, hyperM after 16-cell stage
Histone H3 methylation	ZGA and later	ZGA and later	ZGA and later
Pluripotency transcription factors	OCT4 (POU5F1)	Oct91, -25, -60 (Pou5f3)	Oct4 (Pou5f3)
	SOX2	Sox2	Sox2, Sox19b
	NANOG	Ventx1, -2	Nanog

Download English Version:

https://daneshyari.com/en/article/10799090

Download Persian Version:

https://daneshyari.com/article/10799090

Daneshyari.com