Field:

Biology/Life Science

Session Topic:

Epigenetics

Speaker:

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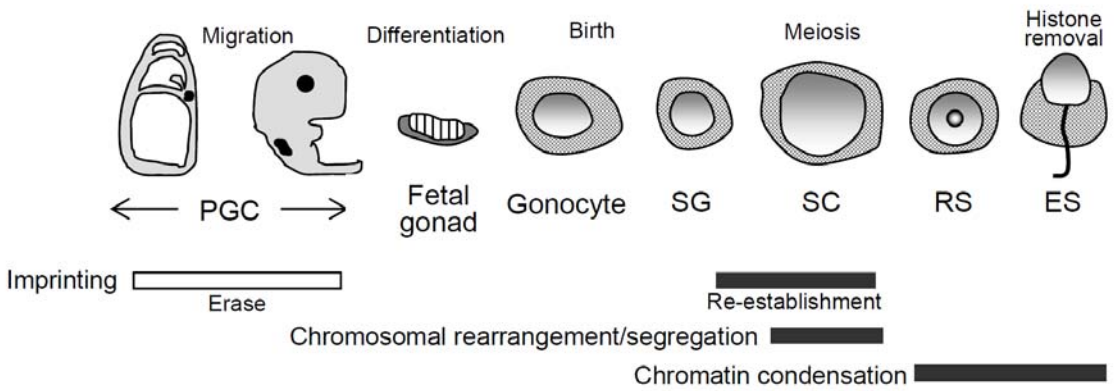
1. Introduction

Unlike genetic regulation, substantial mechanism of epigenetic regulation comprises structural alteration of chromatin composed of DNAs and core-histone octamers (dimers of H2A, H2B, H3 and H4). Several factors have been known to affect the chromatin structure. Among them, histone methylation is the most diverse and complicated modification to modulate the chromatin and subsequent events such as transcription. Until now, there are number of evidences that histone methylation is critical for basic biological activities both in cellular and animal levels, thus impairment of histone methylation and enzymes that catalyze the methylation is highly linked to many types of diseases. Based on my recent research, I here will introduce a significance of histone methylation on male germ cell development through the transcriptional regulation as an example. This regulatory mechanism is also applied for many other tissues and organisms.

2. Histone methylation and spermatogenesis

In mammalian spermatogenesis, serial dynamic and unique genetic/epigenetic events occur such as establishment of imprinting in primordial germ cells, chromosomal rearrangement and segregation during meiosis, and histone removal/chromatin condensation in haploid germ cells (reviewed in ref 1) (Figure). In these events, histone methylation has been shown to play important roles in genome-wide or gene-specific manners. Indeed, knockout mice studies of several histone methyltransferases/ demethylases exhibit impaired spermatogenesis at the various stages. We also reported that removal of certain type of histone methylation was required for pot-meiotic chromatin condensation (Ref 2). Interestingly, recent reports discovered that mature sperm in which histones are replaced and disappeared, still possess small amount of histones, therefore it will be interesting to elucidate the methylation patterns of retained histones in sperm.



3. Epigenetic regulation in spermatogonial stem cells

As mentioned above, the importance of histone methylations at each spermatogenic step has been characterized for years. However, one of these steps has been untouched; the stage of "spermatogonial stem cell (SSC)", although histone methylations are well-studied in other types of stem cells including embryonic stem cells. Recently, we found that one histone methyltransferase is required for maintaining undifferentiated status of SSCs through the global transcriptional activation. Interestingly, the methylation was indispensable only after puberty, implying that epigenetic regulation of SSCs is distinct between child and adult stages. Similar observation was reported in hematopoietic stem cells and neuronal stem cells, but other histone methyltransferase was responsible for these cell types (reviewed in ref 3, 4), thus it's a typical example that various histone methyltransferases cooperate and function as a switch not only spatial but also temporal manner.

4. Perspective

Thanks to a very recent discovery of "epigenetic inheritance over generation" (ref 5-7), epigenetic regulation in germ cells will command more attention from broader fields including biology, medicine, social sciences, etc. In this aspect, JFFOS is one of the best opportunity to discuss about this topic, thus active discussion by attendees with diverse background is appreciated.

References

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