

FUNDING PROGRAM FOR NEXT GENERATION WORLD-LEADING RESEARCHERS

Project Title: Studies about structure and maintenance of sex-specific mammalian epigenome

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1. Background of research

Despite the fact heart cells and brain cells carry the same genes, how do these cells make different tissues and organs? The key is that our cells possess a mechanism that regulate gene-expression during development without any changes of DNA sequences. Moreover, cells also possess a mechanism that maintain gene expression patterns even after cell division. The mechanism that change and maintain gene expression profiles without changes of DNA sequences are called “epigenetics”. Epigenetic machinery play essential roles from fertilization to the grave throughout our life.

2. Research objectives

Many organisms employ sexual reproduction system, that is essential for generation of greater genetic diversity and increasing rate of evolution. To achieve sexual reproduction, Individuals have to differentiate into male or female form sexually undifferentiated zygote. Temporal increase of a sex-determining gene *SRY* during embryogenesis triggers sex differentiation in human. The mechanisms responsible for *SRY*-activation remains unclear. Furthermore, no mutations were found in *SRY*-genes in several cases of human disorders of sex-differentiation. We speculate disorder of epigenetic machinery may cause the failure of temporal *SRY*-expression, at least in some cases. We are planning to reveal the relationship between epigenetic machinery and *Sry*-activation using mice. We are also planning to study the contribution of epigenetic machinery on the maintenance of sex-difference in gonads.

3. Research characteristics (incl. originality and creativity)

Our main purpose is to elucidate the contribution of epigenetic modifier (DNA modifying enzymes, histone modifying enzymes, etc) on sex-differentiation. Since our viewpoint is unique, this research may give novel insight into this field.

4. Anticipated effects and future applications of research

Our goal is an identification of epigenetic modifier that influence sex-differentiation and/or maintenance. The development of inhibitor/activator of the modifier may help the treatment of some disorders of sex-differentiation in the future.