

【Grant-in-Aid for Scientific Research(S)】

Integrated Science and Innovative Science (New multidisciplinary fields)



Title of Project : Analysis of Sex-dependent Epigenome

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Research Area : Basic genome science

Keyword : DNA methylation, T-DMRs, sexual differences, epigenome

【Purpose and Background of the Research】

Epigenetic systems are recognized as memory systems for inheritable gene functions. Epigenome means “total genomic information of epigenetic modifications”. DNA methylation plays a role the main epigenetic regulation mechanism in mammals. A unique feature of the mammalian genome is that there are numerous tissue-dependent and differentially methylated regions (T-DMRs) in non-repetitive sequences, which include genes and their regulatory elements. In mammals, there are at least 200 different cell types based on a variety of physiological and morphological criteria. It is not known if there are T-DMRs that are differentially methylated between male and female animals, other than those found in the sex chromosomes and the genomic regions related to sexual organs development. In this research proposal, we designed a study by analyzing the genome-wide DNA methylation profiles of T-DMRs. We will illustrate “Epigenome Atlas” of cells and tissues of the male and female mice.

【Research Methods】

We have developed D-REAM, a genome-wide DNA methylation analysis method using a high-density genome tiling array, for T-DMR profiling with restriction tag-mediated amplification. In this study, we will analyze tissues (liver, muscle, brain) and cells (ES cells, myoblasts) from intact and castrated male and female mice, by D-REAM.

The experimental plans are as follows:

1. Genome-wide analysis by D-REAM to determine genes with T-DMRs which are differentially methylated between in intact male and female mice.
2. Genome-wide analysis of sex-steroid dependent and independent T-DMRs.
3. Investigation of the epigenetic dynamics of the identified T-DMRs during development and differentiation of stem cells.

【Expected Research Achievements and Scientific Significance】

What is known about the biology of sexual differences is that there are striking differences in the biological functions that can lead to human and animal diseases. Until recently, however, utility of gene sets in the genomic regions are thought to be identical or similar in both sexes, except in sex chromosomes. This research project highlights the epigenome of tissues and cells in male and female respectively. This would be the first trial to investigate sex-dependent epigenome that enables us to identify genes that are differentially regulated due to sexual differences in epigenetic level. There are multiple differences in basic cellular biochemistry of male and female that can affect human health. Information of the T-DMRs would be useful to investigate differences between male and female, providing insights to epigenetic contributions to various chronic human and animal diseases.

【Publications Relevant to the Project】

- Shiota, K., *et al.*, Epigenetic marks by DNA methylation specific to stem, germ and somatic cells in mice. *Genes Cells* 7, 961-969, (2002)
- Yagi, S., *et al.*, DNA methylation profile of tissue-dependent and differentially methylated regions (T-DMRs) in mouse promoter regions demonstrating tissue-specific gene expression. *Genome Res.* 18, 1969-1978, (2008)

【Term of Project】 FY2009-2013

【Budget Allocation】 160,300 Thousand Yen

【Homepage Address and Other Contact Information】

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