

Epigenome Dynamics RIKEN ECL Research Team (2024)

RIKEN ECL Team Leader: Shihori Yokobayashi (Ph.D.)



(0) Research fields

CPR Subcommittee: Biology

Keywords: Human *in vitro* systems, Epigenome heterogeneity, Heterochromatin, Germ cells, Mammalian development

(1) Long-term goal of laboratory and research background

Our life begins as a single cell containing one set of genome information. Epigenome states add an additional layer of information to the genome and enable the generation of various types of cells that form our body. Epigenome states are dynamically regulated during the development of an individual and throughout their life, but to what extent diversity (e.g., cell-to-cell heterogeneity and inter-individual differences) emerges during the establishment and maintenance of an epigenome state is not well understood.

Our research team aims to understand the molecular basis of epigenome heterogeneity that emerged in the human genome. We have previously explored epigenome heterogeneity existing among different human induced pluripotent stem cell (iPSC) lines. Most of the observed heterogeneity was present in regions of low transcriptional activity or non-coding regions, such as repressed promoters, intergenic regions, or repeat elements, with little effect on transcriptional profiles or cell types. In our research, we use such human iPSC lines as a model to assess the behavior of epigenome diversity existing within the same cell type, i.e., considered “epi-polymorphisms.” We aim to understand 1) how epigenome heterogeneity relates to chromatin/nuclear dynamics, 2) how the cellular environment affects epigenome heterogeneity, and 3) how epigenome heterogeneity impacts the changes in cell fate and vice versa. We address these points by integrating epigenome/genome analyses with the other chromatin/omics analyses and *in vitro* differentiation systems for somatic and germ cell lineages. Our study provides insights into understanding the properties of epigenomic diversity among individuals at a molecular level, which will contribute to our understanding of phenotypic diversity and disease susceptibility.

(2) Current research activities (FY2024) and plan

In FY2024, I established my laboratory in August and focused on setting up the research environment, including experimental facilities and equipment, as well as personnel recruitment. We underwent construction associated with necessary laboratory arrangements and set up a designated space for cell culture experiments. One technical staff member was hired.

During this fiscal year, we carried out preparatory work (including evaluation of analytical methods and pilot experiments) for various omics methods aimed at understanding the molecular mechanisms underlying epigenome heterogeneity in human iPS cell lines. In addition, to elucidate how epigenome heterogeneity in human iPS cell lines affects the differentiation process of human primordial germ cell-like cells, we conducted collaborative research with the Institute for the Advanced Study of Human Biology at Kyoto University (my former institution). In parallel, we made various preparations to conduct *in vitro* human germ cell reconstitution experiments at RIKEN.

Going forward, we plan to advance the acquisition of omics data and investigate the relationships across data layers, as well as their impact on *in vitro* germ cell differentiation.

(3) Members

Team Leader: Shihori Yokobayashi
Technical staff I (1)

as of March 2025

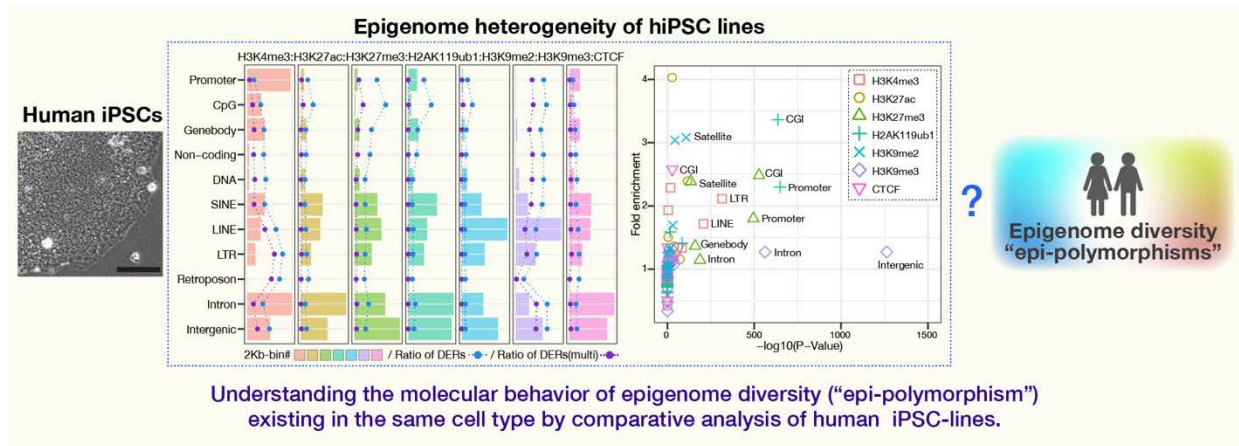
(4) Representative research achievements

1. Yokobayashi S. “Elucidation of epigenome states of human induced pluripotent stem cells and their impact on germ cell differentiation” The 5th Sexual Reproduction Meeting (NIG, Japan) March 2025
2. Yokobayashi S. “Understanding the human germline development using *in vitro* reconstitution systems” Tokyo Metropolitan Institute of Medical Science Seminar (TMiMS, Japan) February 2025
3. Yokobayashi S. “Understanding epigenome reprogramming dynamics in human germ cells using an

improved xenogeneic reconstituted ovary culture” The 47th Molecular Biology Society of Japan (Fukuoka, Japan) November 2024

4. Yokobayashi S. “Elucidation of epigenome states of human induced pluripotent stem cells and their impact on germ cell differentiation” RIKEN IMS Chromatin & Transcription Symposium (IMS) (RIKEN IMS, Japan) November 2024
5. Yokobayashi S. “In vitro gametogenesis using human pluripotent stem cells” Lecture for the Frontier Development Program for Genome Editing, Doctoral Program for World-leading Innovative & Smart Education, Hiroshima University (CiRA, Japan) October 2024

Supplementary



Research Overview

Laboratory Homepage

https://www.riken.jp/en/research/labs/ecl/epigen_dyn_riken_ecl/index.html