Mechanisms of chromatin dynamics at enhancers during ES cell differentiation

Grant Award Details

Mechanisms of chromatin dynamics at enhancers during ES cell differentiation

Grant Type: New Faculty II

Grant Number: RN2-00905

Project Objective: The overall objective is to understand how the chromatin state at enhancers is established and how regulation at these sites contributes to pluripotency of embryonic stem cells.

Investigator:

Name:	Bing Ren
Institution:	Ludwig Institute for Cancer Research
Type:	PI

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $1,726,564

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Reporting Period: Year 5

View Report

Grant Application Details

Application Title: Mechanisms of chromatin dynamics at enhancers during ES cell differentiation

Public Abstract: The human ES cells are euploid cells that can proliferate without limit and maintain the potential to differentiate into all cell types. Differentiation of human ES cells involves selective activation or silencing of genes, a process that involves not only combinatorial interactions between the cis-regulatory sequences and DNA binding transcription factors, but also post-translational histone modifications and other epigenetic mechanisms such as DNA methylation and non-coding RNAs. A number of transcription factors have been found to be essential for the ES cells to maintain their identity or differentiate along specific lineages. These regulators exert their effects through interacting with the promoters, enhancers or silencer elements to modulate the expression of target genes. Currently, the molecular details of how transcription factors modulate target gene expression upon binding to DNA and how they mediate ES cell differentiation are still unclear. The proposed project is aimed to determine the role that histone modifications play in this process. We will conduct experiments to identify the DNA binding proteins, chromatin modifying enzymes and chromatin binding proteins that are responsible for the specific histone modification profiles at regulatory DNA sequences , and investigate how these proteins activate target genes and contribute to the unique properties of human ES cells. Results from the proposed study will improve our understanding of the mechanisms that control pluripotency and lineage specification, and lay a foundation for development of better tools for manipulating and reprogramming human ES cells for regenerative medicine.

Statement of Benefit to California: Our research will provide better understanding of the mechanisms by which human ES cells differentiate along specific cell lineages. Such knowledge will facilitate the development of new methods for manipulating the ES cells, and enable a mechanistic understanding of the reprogramming of somatic cells to the pluripotent state. These results will directly support the efforts by us and other California researchers to investigate the mechanisms of stem cell biology, and design new stem cell therapies.