Title of Project : A research project on the molecular mechanisms of cell fate determination in the cells in which differentiation progresses to multiple pathways in a stepwise manner.

Term of Project : FY2010-2014

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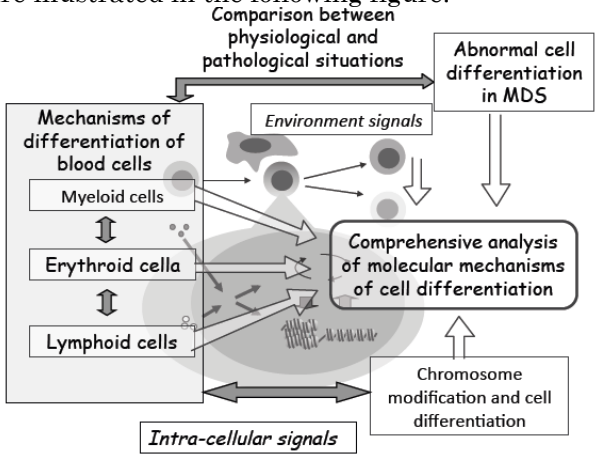
【Purpose of the Research Project】

Recently, it has been demonstrated that forced expression of transcription factors transforms cells to different types of cells. A variety of cells including induced pluri-potent stem cells (iPS cells), neuronal stem cells and monocytes can be generated from fibroblastic cells by expression of combination of transcription factors. However, underlying molecular mechanisms remain elusive. On the other hand, normal process of differentiation is usually irreversible. This was clearly demonstrated in hematopoietic system. The main purpose of this research project is to clarify the molecular mechanisms of differentiation of the cells from various points of views including chromosome modification, transcriptional control and cell-cycle control.

【Content of the Research Project】

The contents of the research projects are illustrated in the following figure.



Molecular mechanisms underlying cell differentiation will be investigated mainly using hematopoietic cells. While in hematopoietic system, differentiation of myeloid, erythroid and lymphoid cell lineages will be studied, differentiation of other cell lineages may be also included in the whole research project.

Differentiation control by environmental niches will be also studied. In addition to differentiation of normal cells, pathological cells with abnormal/disrupted differentiation are investigated in comparison with normal cells. In particular, we focus on a disease called myelodysplastic syndromes (MDS) where normal process of differentiation is disrupted by unknown reason. MDS is a disease resistant to therapies, and frequently progresses to overt leukemia. However, interestingly, it has been demonstrated that 40-50% of MDS patients responded to hypomethylating drugs such as 5-Aza C, implicating decreased gene expression caused by epigenetic abnormality in MDS.

Thus, we investigate normal process of differentiation as well as differentiation under pathological situations to clarify the molecular mechanisms of cell differentiation through analyzing chromosome modification and transcriptional control.

【Expected Research Achievements】

Clarification of molecular mechanisms of cell differentiation in relation to chromosome modification and transcriptional control.

【Key Words】

Cell differentiation
Chromosome modification
Transcriptional regulation
Cell-cycle control
Hematopoietic cells
DNA methylation
Epigenetics
Retrovirus vector technology

【Homepage Address】

http://www.riken.jp/cell-fate/