Elucidation of the differentiation mechanism of stem cells and ES cells and establishment of control method

Stem cells, cell differentiation, regenerative medicine, hematopoietic cells, germ cells

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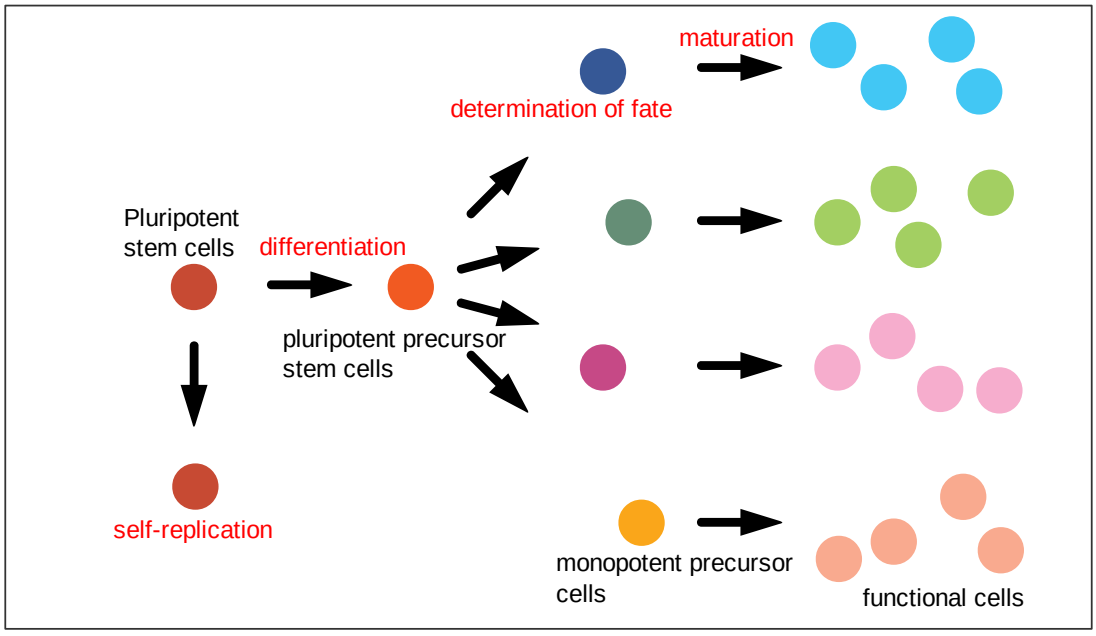
1 What is a stem cell?

Stem cells are undifferentiated cells with auto-replication ability and differentiation potential. Stem cells are destined for various cell systems, and mature and finally differentiate into functional cells. Cells with a short life span such as blood cells and epithelial cells of skin and intestinal mucosa do not exhaust because stem cells of the cell types continuously generate new cells.
It has recently been clarified that stem cells are present in tissues, which has previously been considered not to regenerate, such as nerves and skeletal muscle. Our bodies are a 'stem cell world' consisting of many stem cell systems.

Stem cells have rapidly acquired recognition because stem cell transplantation after amplification in vitro utilizing its replication potential is expected for regenerative medicine. In our research field, we are performing basic studies of the items below for the main subjects of the mechanism of stem cells formation and application of stem cells for regenerative medicine by manipulation of the cells.



- Stem cells have self-replication ability and differentiation potential.
- Stem cells finally differentiate into functional cells through determination of fate and maturation.

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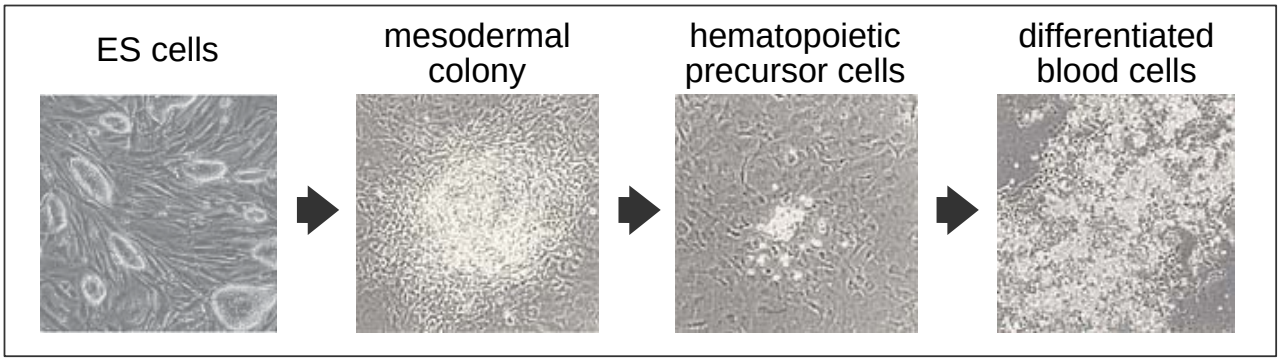
2 Induction of differentiation of ES cells into blood cells

In addition to organ-specific stem cells, there are embryonic stem (ES) cells established from early embryo. When mouse ES cells are returned to early embryo, the cells are incorporated into the normal development process, and differentiate into all types of cells including germ cells. Thus, ES cells are omnipotent in differentiation.

Differentiation potential in vitro is quite limited, compared to that in vivo. However, differentiation into blood cells, vascular endothelial cells, cardiac muscle cells, and neurons is readily induced.
We developed a method of inducing blood cell differentiation (OP9 system) by culturing mouse ES cells on stroma cells. We are analyzing the molecular mechanism of blood cell differentiation and studying its application for regenerative medicine.



- Differentiation of ES cells into functional blood cells through mesodermal colony and hematopoietic precursor cells can be induced by culturing ES cells on stroma cells OP9.
- Conditional expression of a specific gene in this differentiation induction process is possible.
- The hematopoiesis mechanism can be clarified by various genetic manipulations.

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3

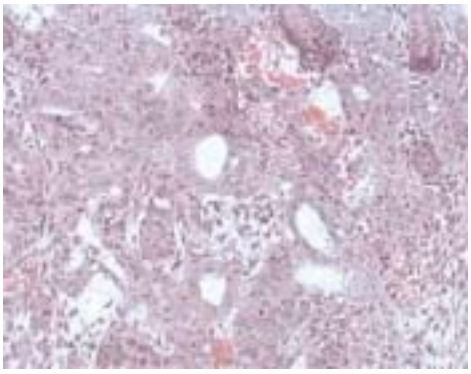
Establishment mechanism of germ cells and stem cells

Our bodies consist of germ cells capable of transmitting genetic information to the next generation and other somatic cells. Germ line cells separate from somatic cells and differentiate in the early step of embryogenesis.

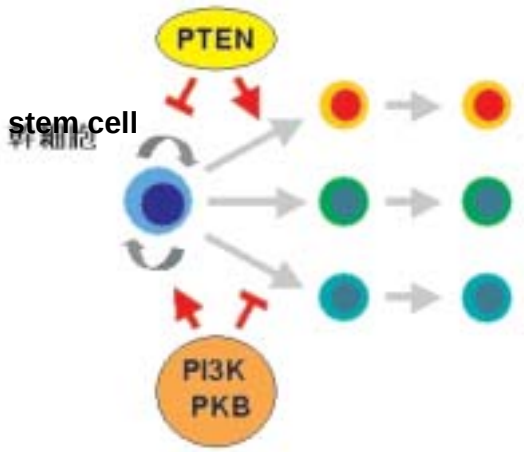
Cells called primordial germ cells that first appear in that process have already been destined for the germ line, but dedifferentiation into omnipotent embryonic germ (EG) cells with properties similar to those of ES cells occurs under specific culture conditions.

We are studying how germ line cells are destined, and how germ line cells re-acquired the omnipotency.
Through this study, we are also investigating how omnipotency of cells is established.
Based on analysis of knockout antioncogene PTEN, we consider that the signal of PTEN/PI3 kinase acts for maintenance of the undifferentiated state of stem cells.

We are studying the relationship of PTEN/PI3 kinase with 'stem cell properties' and developing a stem cell control method using manipulation of signals.



PTEN defect-associated teratoma



- Defect of antioncogene PTEN induces 'dedifferentiation' of germ cells into omnipotent precursor cells.
- PTEN and PI3 kinase signals have important function for maintenance of stem cells.

Other study contents of Nakano laboratory
- Functional analysis of PGC7/Stella in establishment of germ cells
- Yesterday analysis of mammalian Piwi family genes