Development of genetically engineered PA6 feeder cells for neural differentiation of mouse and human iPS cells

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論 文 名　：Development of genetically engineered PA6 feeder cells for neural
　　　　　　differentiation of mouse and human iPS cells
　　　　　　（マウスおよびヒトiPS細胞の神経分化のための遺伝子改変PA6フィーダー細胞
　　　　　　の開発）

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論　文　内　容　の　要　旨

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The neurodegeneration of the CNS is caused by chronic, progressive disorders caused by the gradually loss of neurons in the central nerve system (CNS). However, the CNS, which controls the activities of the body, in vertebrates lack of ability to regenerate. As the elderly population has increased in recent years, the age-related neurodegenerative diseases are becoming increasingly prevalent. Neurodegenerative diseases like Alzheimer's disease and Parkinson's disease not only affect patience's behavior, memory, language, but also every organ in the body. Since, CNS of vertebrate lack of regenerative ability, rescue the remaining neurons, increase the number of neurons or replace the lost neurons became the potential therapeutic strategies for treating neurodegenerative diseases.

Regenerative medicine, especially stem cell technology, take advantages of the body's natural ability to heal itself, offers realistic way to restore diseased, injured tissues and whole organs. By this, regenerative medicine can not only relieving patience's symptoms, but addressing the root cause of the pain. Pluripotent stem cells including embryonic stem (ES), induced pluripotent stem (iPS) cells are characterized by self-renewal and differentiation potential for all cell types, which lead pluripotent stem cells become a frontline source of regenerative medicine. Therefore, to study early neural development and also offer a potential source of cells for nerve regeneration, investigating neural differentiation of ES/iPS cells is of important significance. Stromal cell-derived inducing activity (SDIA) using mouse stromal PA6 cells promotes neural differentiation of iPS cells.

In Chapter 1, general knowledge about neurodegenerative diseases, and the most promising way to cure these diseases - regenerative medicine, particularly stem cells, are introduced. In addition, the research purpose and strategy of the study in this thesis are briefly introduced.

In Chapter 2, a literature review for the techniques and mechanisms related to the neural induction of ES/iPS cells were conducted. General techniques which has been used for neural induction of ES/iPS cells, such as EB formation, SMs and TFs addition, the main method that be used in this study – SDIA method were included. Furthermore, one of the important CAM – cadherin, which had been genetically engineered into PA6 feeder cells to improve neural induction of PA6 cells in the current study, was also reviewed.

In Chapter 3, a study on neural differentiation of mouse iPS cells by co-culturing with genetically modified Dox inducible cadherin over-expressing cells is demonstrated, which feeder significantly improved neural differentiation efficiency of mouse iPS cells compared with parental PA6 cells.

In Chapter 4, mouse and human iPS cells were co-cultured with an improved feeder cells, constitutively

E-cadherin expressing cells. New feeder showed improved enhancement of neural differentiation efficiency of both mouse and human iPS cells.

In Chapter5, the contents of this and future perspective are summarized.