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人工多能性幹細胞(iPS 細胞)を用いた神経変性疾患研究

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Recent advances in modeling neurological disorders using induced pluripotent stem cells

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要旨

ヒト iPS 細胞の樹立は, Oct3/4, Sox2, Klf4, c-Myc の 4 遺伝子をレトロウィルスにより導入することにより実現された. この細胞は元となった細胞の遺伝情報を引き継いでおり, また 3 胚葉系それぞれへの分化能をもつため, 様々な疾患の病態研究へ応用することができる. このように, 患者由来の iPS 細胞より疾患標的細胞への分化が可能になったことで, 多くの疾患再現の試みがなされてきている. 神経・筋疾患では, 原因遺伝子の要因が大きな比重を占める脊髄性筋萎縮症や家族性自律神経失調症由来の iPS 細胞でいち早く疾患再現が報告された. 今後, パーキンソン病やアルツハイマー病など, 患者の大部分が孤発性であり, 遺伝的な原因が不明であるこれらの疾患についても, 患者由来の iPS 細胞の解析が進むことが期待される. 移植への応用に関しては, 腫瘍形成の可能性という課題がある. 鳥取臨床科学 4(1), 75-78, 2011

Abstract

Induced pluripotent stem (iPS) cells are generated from adult human somatic cells by the retrovirus-mediated transduction of four transcription factors, namely Oct3/4, Sox2, Klf4 and c-Myc. iPS cells inherit the genetic background of donor somatic cells and can differentiate into all three germ layers; therefore, iPS cells can be used for studies of various diseases. iPS technology has opened an avenue to generate disease-specific pluripotent stem cells that can differentiate into specific types of cells (disease-targeted cells) that are significantly involved in disease mechanisms, thereby, iPS cells can be a disease model used for understanding disease mechanisms, drug screening and toxicology. Modeling neurological diseases with human iPS cells first succeeded in early-onset neurological diseases, including spinal muscular atrophy and familial dysautonomia, which are mostly triggered by gene mutation. For late-onset neurodegenerative disorders, such as Parkinson's and Alzheimer's diseases, where most patients are sporadic and the genetic background is unclear, iPS cells will be generated from the patients and tested as to whether they can be applied to modeling of such late-onset diseases. The application of iPS cells to transplantation therapies involves hurdles awaiting solution, such as tumor formation. Tottori J. Clin. Res. 4(1), 75-78, 2011

Key Words: 人工多能性幹細胞(iPS 細胞), 疾患標的細胞, 神経疾患, パーキンソン病, アルツハイマー病, 移植医療; induced pluripotent stem cells, disease-targeted cells, neurological disorders, Parkinson's