第51回 日本神経学会総会

ランチョンセミナー12

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Opportunities for neurorestorative therapies in PD using iPS and stem cells

座 長

京都大学大学院医学研究科 臨床神経学（神経内科）教授
高橋 良輔 先生

演 者

Ole Isacson, M.D, Dr.Med.Sci
Professor. Director, Center for Neuroregeneration Research,
McLean Hospital/ Harvard Medical School, Belmont, USA,
and NIH Udall Parkinson's Disease Research Center of Excellence

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会 場

東京国際フォーラム ホールB-7（2） [第4会場]

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Biosketch

Dr. Ole Isacson is Professor of Neurology (Neuroscience) at Harvard Medical School and Director of the Center for Neuroregeneration Research and the Neuroregeneration Laboratory at McLean Hospital, an NIH Udall Parkinson's Disease Research Center of Excellence. He is also a member of the Scientific Advisory Board of the Harvard NeuroDiscovery Center and Principal Faculty of the Harvard Stem Cell Institute. Since 1990, Dr. Isacson's laboratory has grown to an internationally recognized academic research center for Parkinson's disease and related disorders. He is a founding member and past President of the American Society for Neural Therapy & Repair, and the past President of the international Cell Transplant Society, CTS (branch of The Transplantation Society, TTS). Dr. Isacson has received several international prizes, research awards and lectureships. He is author or co-author of over 250 scientific research articles and 3 books in his field. He is the Editor-in-Chief of the journal, *Molecular and Cellular Neuroscience.*

Ole Isacson, M.D, Dr.Med.Sci

Abstract

Cell therapy for the Parkinson's disease (PD) has advanced significantly in recent years. Open-label clinical trials have provided proof of principle that transplantation of fetal DA neurons can improve patients' neurological motor symptoms. It is likely in the near future that technical improvements, including standardization in fetal cell preparation and delivery, will provide more reliable clinical outcome and reduce the risk of side effects. However, fetal cell therapy is only an experimental procedure, and depends on complex issues for access to rare donor cells. Stem cell derived neurons may provide a more practical source of neurons for future cell therapy and transplantation in PD. Early work from our laboratories demonstrated that mouse embryonic stem (ES) cell derived dopamine (DA) neurons restored striatal DA storage capacity and cortical motor activation as measured by PET and functional magnetic resonance imaging in animal models of PD. A gradual recovery of motor function reflected the differentiation and maturation of synaptic connections of the transplanted DA neurons. Since these discoveries, human ES cell differentiation protocols have been developed for in vitro differentiation increasing the yield of the authentic human ventral midbrain neurons in vitro, and these neurons can also be implanted in animal models with functional effects. A major concern in ES-derived neural transplantation is the potential risk of tumor formation. We have developed cell sorting and other protocols to eliminate such risk. For example, fluorescence activated cell sorting, initially developed for hematological research and analysis, can be successfully adapted to select the progeny of human ES cells on the basis of expression of specific cell-surface markers. Alternatives to human ES cells as sources of donor cells have emerged through manipulation of adult cells, including fibroblasts, with various transcription factors. A very promising approach involves controlled de-differentiation (reprogramming) adult cells to become ES-like, also known as induced pluripotent stem (iPS) cells. iPS cells can be produced by various methods, for example by the expression of the transcription factors Oct-4, Sox2 and and Klf4 in adult fibroblasts until an ES-cell state of gene-expression is obtained. Large scale derivation and differentiation of functional human DA neurons with the authentic midbrain neuronal phenotype from PD patient iPS cells is now made possible by improved protocols. Such cells not only provide a future cell source for cell therapy, but also represent a major new research tool in neuroscience, neurology and development of new medicines. The exceptional pace of innovation in this iPS cell and therapy field will continue help drive the emerging field of regenerative medicine to accomplish significant future advances.