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学 位 論 文 の 内 容 の 要 旨

Dissertation Abstract

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(学位論文のタイトル)

Transplantation of iPS-derived Vascular Endothelial Cells Improves White Matter Ischemic Damage

(ヒトiPS細胞から作り出した血管内皮細胞の移植で動物モデルの脳白質梗塞が劇的に改善)

(学位論文の要旨)

White matter infarct induces demyelination and brain dysfunction. We previously reported that transplantation of brain microvascular endothelial cells improved the behavioral outcome and promoted remyelination by increasing the number of oligodendrocyte precursor cells in the rat model of white matter infarct. In this study, we investigated the effects of transplantation of vascular endothelial cells generated from human induced pluripotent stem cells (iPSCs) on the rat model of white matter infarct. Seven days after induction of ischemic demyelinating lesion by injection of endothelin-1 into the internal capsule of a rat brain, iPSC-derived vascular endothelial cells (iVECs) were transplanted into the site of demyelination. The majority of iVECs transplanted into the internal capsule survived for 14 days after transplantation when traced by immunohistochemistry for a human cytoplasmic protein. iVEC transplantation significantly recovered hind limb rotation angle as compared to human iPSC or rat meningeal cell transplantation when evaluated using footprint test. Fourteen days after iVEC transplantation, the infarct area remarkably decreased as compared to that just before the transplantation when evaluated using magnetic resonance imaging or luxol fast blue staining, and remyelination was promoted dramatically in the infarct when assessed using luxol fast blue staining. Transplantation of iVECs increased the number of oligodendrocyte lineage cells and suppressed the inflammatory response and reactive astrogliogenesis. These results suggest that iVEC transplantation may prove useful in treatment for white matter infarct.