Received: 7 June 2017 | Revised: 18 September 2017 | Accepted: 18 October 2017

DOI: 10.1002/jnr.24197

RESEARCH ARTICLE

WILEY

Transplantation of feeder-free human induced pluripotent stem cell–derived cortical neuron progenitors in adult male Wistar rats with focal brain ischemia

Yulius Hermanto[1,2,3] | Tadashi Sunohara[1,2] | Ahmad Faried[3] | Yasushi Takagi[4] | Jun Takahashi[2] | Takakuni Maki[5] | Susumu Miyamoto[1]

[1]Department of Neurosurgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

[2]Department of Clinical Application, Center of iPS Cell Research and Application, Kyoto University, Kyoto, Japan

[3]Department of Neurosurgery, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia

[4]Department of Neurosurgery, Institute of Biological Sciences, Tokushima University, Tokushima, Japan

[5]Department of Neurology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Correspondence
Yasushi Takagi, Department of Neurosurgery, Institute of Biological Sciences, Tokushima University. 3-8-15, Kuramoto-cho, Tokushima, 770-8503, Japan.
Email: ytakagi@tokushima-u.ac.jp

Funding Information
This study was supported by a grant from the Network Program for Realization of Regenerative Medicine from the Japan Agency for Medical Research and Development and an Intramural Research Grant for Neurological and Psychiatric Disorders from the National Center of Neurology and Psychiatry.

Abstract

The use of human induced pluripotent stem cells (hiPSCs) eliminates the ethical issues associated with fetal or embryonic materials, thus allowing progress in cell therapy research for ischemic stroke. Strict regulation of cell therapy development requires the xeno-free condition to eliminate clinical complications. Maintenance of hiPSCs with feeder-free condition presents a higher degree of spontaneous differentiation in comparison with conventional cultures. Therefore, feeder-free derivation might be not ideal for developing transplantable hiPSC derivatives. We developed the feeder-free condition for differentiation of cortical neurons from hiPSCs. Then, we evaluated the cells' characteristics upon transplantation into the sham and focal brain ischemia on adult male Wistar rats. Grafts in lesioned brains demonstrated polarized reactivity toward the ischemic border, indicated by directional preferences in axonal outgrowth and cellular migration, with no influence on graft survival. Following the transplantation, forelimb asymmetry was better restored compared with controls. Herein, we provide evidence to support the use of the xeno-free condition for the development of cell therapy for ischemic stroke.

KEYWORDS
cell therapy, human pluripotent stem cells, ischemic stroke, neural stem cells

1 | INTRODUCTION

Ischemic stroke gives rise to adult disability worldwide (George & Steinberg, 2015; Moskowitz, Lo, & Iadecola, 2010). Transplantation of human neural stem cells (NSCs) has been reported to improve functional recovery in animal models of stroke (Andres et al., 2011; Gomi et al., 2012; Mine et al., 2013; Oki et al., 2012; Tornero et al., 2013). Clinical trials of human NSC transplantation had been conducted in limited numbers of patients with few sensorimotor improvements (Kalladka et al., 2016; Kondziolka et al., 2005). Human induced pluripotent stem cells (hiPSCs) represent a valuable treatment option for stroke because the use of hiPSCs avoids many of the ethical issues associated with the use of fetal or embryonic material (Takahashi et al., 2007).

Significance

Cortical neurons could be induced under the feeder-free condition from hiPSCs. The cells also could survive, migrate, differentiate, and undergo axonal outgrowth upon transplantation in adult male Wistar rats with focal brain ischemia.

