Autologous transplantation shows promising results for iPS cell therapy in Parkinson's disease

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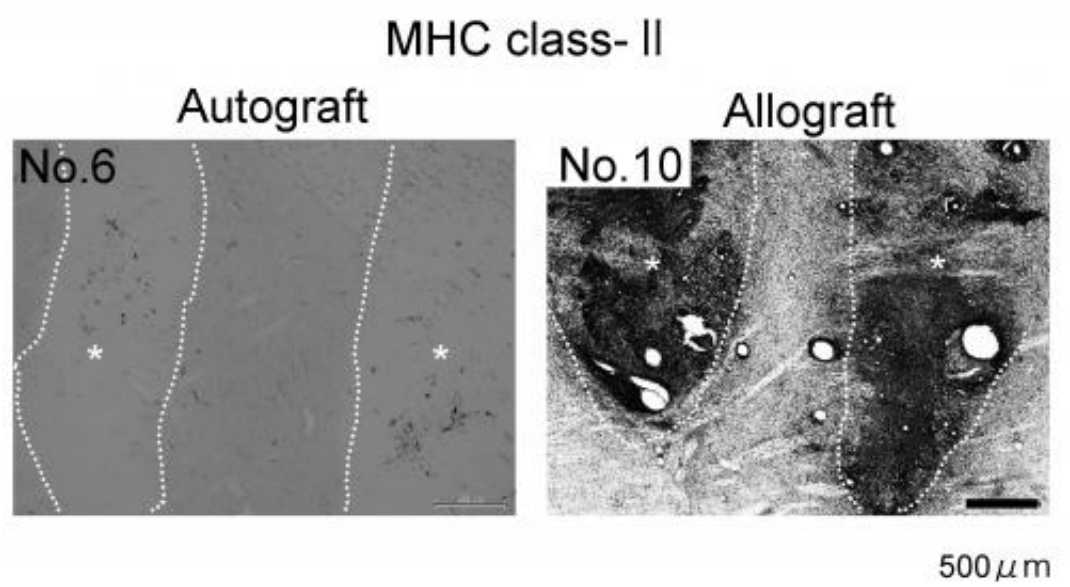


This is a histological analysis of the host-resident microglia. Dark parts of the photo No.10 (right) shows microglia gather in the brain. Credit: Dr. Asuka Morizane

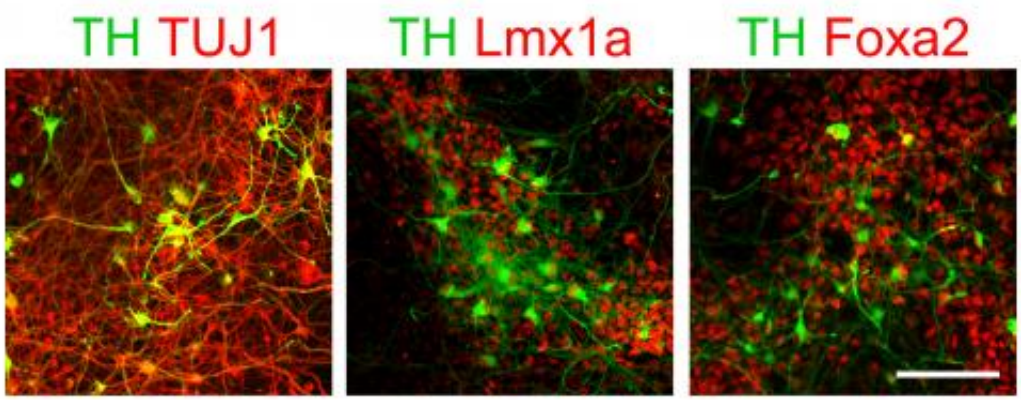
A research team led by Professor Jun Takahashi and Assistant Professor Asuka Morizane at the Center for iPS Cell Research and Application (CiRA) at Kyoto University, Japan, has carried out a study to compare the impact of immune response in autologous transplantation

(transplantation of cells from the subject's own body) and allogeneic transplantation (transplantation of cells from a different individual of the same species). The researchers used cynomolgus monkeys to carry out transplantation into the brain of neural cells derived from iPS cells. Autologous transplantation was found to produce almost no immune reaction and to result in viable neural cells. By contrast, allogeneic transplantation provoked immune reaction by microglia and lymphocytes.

Parkinson's disease is a progressive and intractable disease of the nervous system in which the loss of dopaminergic neurons in the brain leads to reduced dopamine production, resulting in limb tremor, stiffness causing difficulty in movement, and other symptoms. The therapies applied up till now, based on drugs or electrode treatment, may improve symptoms but have proved unable to halt the depletion of dopaminergic neurons. Hopes have therefore become focused on a therapy with the more radical approach of replacing the lost neural cells through cell transplantation, thereby promoting the formation of new neural pathways to restore brain function. Human iPS cells are looked to as a potential source of the transplant cells.

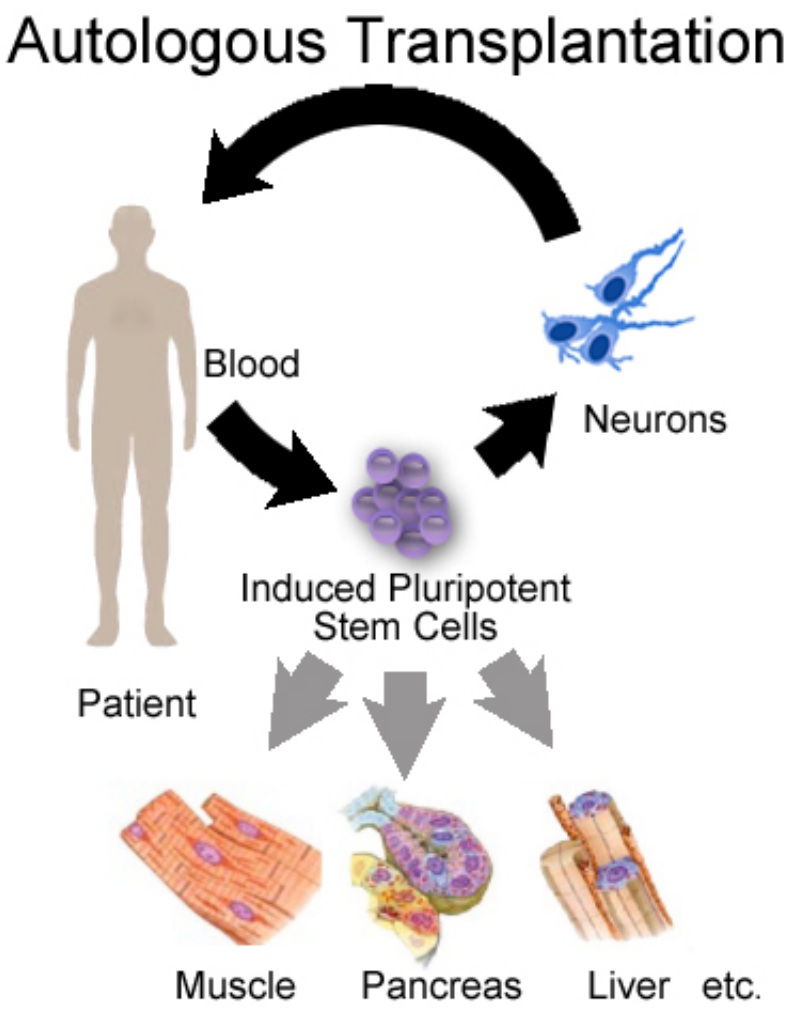
It is hoped that iPS cells will make it possible to use cells derived from the transplant patients themselves to perform autologous transplantation. If autologous transplantation could allow immune reaction to be avoided, it would also make unnecessary the use of immunosuppressant drugs and avert the risk of side-effects caused by immunosuppression. However, the studies of iPS cell-based autologous transplantation carried out so far, which have used a mouse model, have produced no firm conclusion, with immune reaction observed in some studies but not in others. Moreover, these studies did not involve transplantation of differentiated cells derived from iPS cells in a way that mimicked clinical application. There had thus been no studies directly investigating the effect of autologous transplantation and allogeneic transplantation in primates.

This study by Dr. Takahashi's group sought to clarify this area by transplanting dopaminergic neurons prepared from iPS cells into the brains of cynomolgus monkeys and comparing the extent of immune reaction between autologous and allogeneic transplantation.



This is an immunostaining of primate iPSC-derived neurons on day 39. Green colors shows dopaminergic neural cells. Credit: Dr. Asuka Morizane

iPS cells prepared from four cynomolgus monkeys were differentiated into dopaminergic neural cells over a period of 28 days and transplanted into the monkeys' brains, which were observed over a period of approximately three months during which no immunosuppressants were used. The study data show that, in primates, autologous transplantation of iPS cell-derived neural cells produces almost no immune reaction and is superior to allogeneic transplantation in terms of immune reaction control and cell viability.



This illustration shows the image of autotransplantation. The paper shows evidence only for neural cells and the brain, not for other organs. Immunogenicity in other organs needs to be explored. Credit: *Stem Cell Reports*, Morizane et al

More information: "A direct Comparison of Autologous and Allogeneic Transplantation of iPSC-Derived Neural Cells in the Brain of a Nonhuman Primate" *Stem Cell Reports*, 2013. dx.doi.org/10.1016/j.stemcr.2013.08.007

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