“Cell therapy using human iPSC-derived renal progenitors ameliorates acute kidney injury in mice” published in “Stem Cells Translational Medicine” on line

Tokyo, July 22, 2015 - Astellas Pharma Inc. (Tokyo: 4503; “Astellas”) and Prof. Osafune’s group of Center for iPS Cell Research and Application (Director: Dr. Shinya Yamanaka; “CiRA”), Kyoto University, as an achievement of their collaborative research for kidney regenerative medicine, published a research paper in “Stem Cells Translational Medicine” on line (9:00 EST, July 21).

Summary
- New method for generating renal progenitors from human induced pluripotent stem cells (hiPSCs) was established
- Transplantation of human iPSC-derived renal progenitors ameliorated acute kidney injury (AKI) in mice
- Cell therapy using the hiPSC-derived renal progenitor cells could be developed for kidney diseases

The research group found that transplantation of human iPSC-derived renal progenitors suppressed the renal dysfunction and histopathological changes associated with AKI in mice.

AKI is defined as a rapid loss of renal function resulting from various etiologies, with a mortality rate exceeding 60% among intensive care patients. Because conventional treatments have failed to alleviate this condition, a new innovative treatment option such as regenerative therapies is strongly anticipated. In this February, Italian research group reported that transplantation of human iPSC-derived renal progenitors via the tail vein ameliorated renal injury in a cisplatin-induced AKI mouse model.

Transcription factors, Osr1 and Six2 interact synergistically to maintain nephron progenitor status during kidney organogenesis, and the combination of Osr1 and Six2 can be used as a specific marker set to define nephron progenitors. The research group has established a novel protocol to efficiently differentiate hiPSCs into OSR1+SIX2+ renal progenitors, and demonstrated the progenitors were able to form proximal renal tubule-like structures in vitro and in vivo. Moreover, in ischemia/reperfusion-induced AKI mouse model, renal subcapsular transplantation of these cells significantly suppressed the elevation of blood urea nitrogen and serum creatinine levels and attenuated histopathological changes, such as tubular necrosis,
tubule dilatation with casts, and interstitial fibrosis.

This is the first report to demonstrate that the transplantation of renal progenitor cells differentiated from human iPSCs have therapeutic efficacy in the AKI mouse model induced by ischemia/reperfusion. No engraftment of transplanted renal progenitor cell indicates that trophic factors secreted from the cells exerted reno-protective effects on the host kidney.

These findings therefore suggest that cell therapy using hiPSC-derived renal progenitors might become one of therapeutic options for AKI patients by ameliorating renal tissue damage and possibly preventing transition to chronic tissue damage. Based on the findings, Astellas and CiRA will explore the possibility to develop new cell-based therapies for not only AKI but also chronic kidney disease (CKD).

Title of Paper
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Journal
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About the Center for iPS Cell Research and Application at Kyoto University (CiRA)
CiRA is working to build an iPS cell stock, which preserves clinical-grade iPS cells generated from HLA homozygous donors in order to realize iPS cell-based cell therapy.
CiRA researchers are also preparing clinical research on various diseases including Parkinson’s disease and blood diseases. Additional information about CiRA is available through its website at www.cira.kyoto-u.ac.jp.

Astellas initiatives in regenerative medicine research
Astellas is currently engaged in research activities using iPS cells as well as somatic stem cells. The company focused attention on iPS technology in the early days of its invention, and
participated in the Project for Accelerating Clinical Application of iPS cells along with making strategic investment in venture companies. Newly established Regenerative Medicine Labs will serve as a hub to further promote collaboration with academic institutions to realize early clinical application of regenerative medicine products.

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