Astellas and CiRA, Kyoto University discover efficient methods of differentiating nephron progenitor cells from human iPS/ES cells

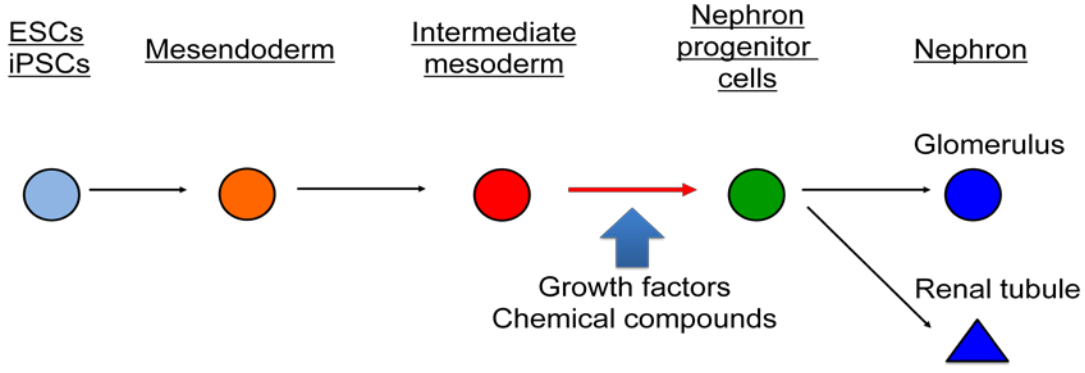
- Presented at ISSCR's 11th Annual Meeting –

Tokyo, June 18, 2013 - Astellas Pharma Inc. (Tokyo: 4503; "Astellas") and Kyoto University's Center for iPS Cell Research and Application (Director: Dr. Shinya Yamanaka; "CiRA"), as a part of their collaborative research for kidney regenerative medicine, discovered methods of efficiently carrying out one of the processes in which kidneys are regenerated from human induced pluripotent stem cells (iPS cells) and human embryonic stem cells (ES cells), and presented the discovery at the International Society for Stem Cell Research's (ISSCR) 11th Annual Meeting (held in Boston from June 12 to 15, 2013).

The development of kidney regenerative medicines is desirable in order to contribute to the treatment of chronic renal failure and other refractory renal diseases. There is currently no effective treatment for refractory renal diseases, and more people are expected to suffer from these diseases as the society continues to age. Although kidney transplantation is only one curative treatment for these diseases, the shortage of donors remains an unresolved issue.

Astellas has been involved in collaborative research for kidney regenerative medicine with a research group at Kyoto University's CiRA led by Associate Professor Dr. Kenji Osafune, a leading researcher of kidney regeneration from iPS cells. A part of this research effort is to generate cells which are cellular components of nephron (the functional unit of kidneys) from pluripotent stem cells such as human ES and iPS cells, and apply this to drug discovery and regenerative medicine. Dr. Kenji Osafune's group established methods of efficiently generating intermediate mesoderm, which occurs in the course of kidney development (Mae S et al., Nat Commun, 2013). This research group and Astellas have now developed efficient methods of differentiating nephron progenitor cells from the intermediate mesoderm by treating it with various growth factors and chemical compounds.

Analysis of the nephron progenitor cells differentiated in these methods proved that they have the characteristics of genuine nephron progenitor cells in the body, including the expression of various genes specific to human nephron progenitor cells, the potential to develop into cellular components of nephron, and the formation of three-dimensional tubular structures with protein expression specific to renal tubule *in vitro* and *in vivo*.



The results suggest that these differentiation methods can induce human iPS/ES cells into nephron progenitor cells with similar developmental potentials to those in embryos. In the future, Astellas and CiRA will further develop methods of generating nephron cells, components of glomerulus and renal tubule from nephron progenitor cells, and will apply them to the development of therapeutic medicines through evaluation of drug candidates and preparation of disease models, and further open the door for the development of new cell-based therapies for the treatment of kidney diseases as a curative therapy.

As announced in May 2013, Astellas will expand its commitment to regenerative medicine and make a full commitment to cell therapy over and above the regenerative drugs R&D conducted to date. Astellas will also promote research using somatic stem cell technology in addition to that of iPS cells. Taking advantage of these new results, Astellas will aim to realize innovative cell therapies.

About kidneys and nephrons

Kidneys remove bodily wastes from blood and excrete them into urine and serve the role of maintaining water and electrolyte balance in the body, as well as other physiological functions such as blood pressure regulation, hematopoiesis, and regulation of bone metabolism. Nephron is the functional unit for producing and excreting urine, which has glomerulus and renal tubules that contribute to that function. In renal failures, nephrons are damaged and lose their functions.

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