【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project : Kidney reconstitution and disease modeling based on nephron induction methods in vitro

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Research Project Number : 17H06177 Researcher Number : 70291309
Research Area : Nephrology, Developmental Biology
Keyword : Kidney development, iPS cell, nephron progenitor

【Purpose and Background of the Research】

The kidney develops through the interactions of three precursor tissues: nephron progenitors, ureteric buds, and stromal progenitors. We have previously reported the induction method of nephron progenitors from multipotent stem cells. One of the aims of this project is to induce the ureteric bud in addition to nephron progenitors, and utilize these methods to reveal mechanisms underlying the hereditary kidney diseases. The other aim is to induce the stromal progenitors and combine them with nephron progenitors and the ureteric bud to generate the genuine three-dimensional kidney structures.

【Research Methods】

We will establish methods to induce the ureteric bud and stromal progenitors from mouse ES cells, and subsequently from human iPS cells. We then apply the methods to the iPS cells derived from hereditary kidney diseases, to model the phenotypes and reveal mechanisms underlying the diseases. We will also establish a method to combine the three progenitors to reconstitute the genuine three-dimensional kidney structures from mouse ES cells, and eventually from human iPS cells.

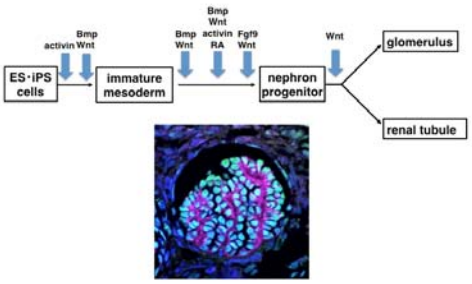

Figure 1 Renal glomerulus generated in vitro

【Expected Research Achievements and Scientific Significance】

Easy and frequent access to human kidney tissues will accelerate the human developmental nephrology and reveal the species differences from other animal models including mice. In addition, elucidation of the mechanisms of the hereditary kidney diseases will serve as basis for drug screening aiming at the treatment. Furthermore, generation of the three-dimensional kidney structures will advance the regenerative medicine toward the renal transplantation of the induced organs in the future.

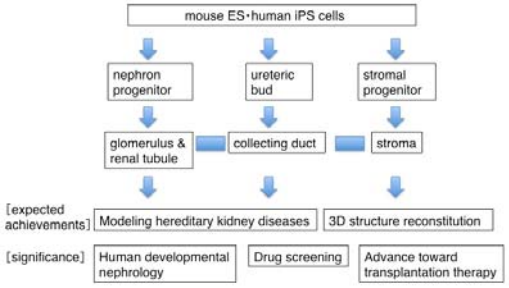

Figure 2 Expected achievements and significance

【Publications Relevant to the Project】

・Sharmin S, Taguchi A, Kaku Y, Yoshimura Y, Ohmori T, Sakuma T, Mukoyama M, Yamamoto T, Kurihara H, and Nishinakamura R. Human induced pluripotent stem cell-derived podocytes mature into vascularized glomeruli upon experimental transplantation. **J Am Soc Nephrol** 27: 1778-1791, 2016
・Taguchi A, Kaku Y, Ohmori T, Sharmin S, Ogawa M, Sasaki H, and Nishinakamura R. Redefining the in vivo origin of metanephric nephron progenitors enables generation of complex kidney structures from pluripotent stem cells. **Cell Stem Cell** 14: 53-67, 2014

【Term of Project】 FY2017-2021

【Budget Allocation】 157,100 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.imeg.kumamoto-u.ac.jp/en/bunya_top/kidney_development/