


## Creating a kidney: A global network to generate transplantable kidney organoids

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### Purpose and Significance of the Research

#### ● Creating transplantable human kidney organoids

Approximately 10% of the world's population suffers from chronic kidney disease, and more than 2 million people are undergoing artificial dialysis or kidney transplantation. However, there is no curative treatment and an overwhelming shortage of kidney transplant donors. Artificial kidneys with complex structures and functions were considered a pipe dream, but the tide turned in 2014 when we succeeded in producing human kidney organoids. While the kidney organoid technology has been proved useful for disease modeling and search for therapeutic drugs (Figure 1), the currently available organoids still lack the complete organotypic structure and their functions are insufficient. Therefore, this project aims to **produce next-generation kidney organoids and functional maturity for clinical transplantation in the future**. By bringing together diverse and cutting-edge methods of human embryology, microdevices, novel whole embryo culture systems, and in vivo organ production, we aim to create more mature and functional implantable kidney organoids (Figure 2). To this end, five domestic and five foreign researchers will form a strong international research network in which young researchers can move freely and grow into leaders.

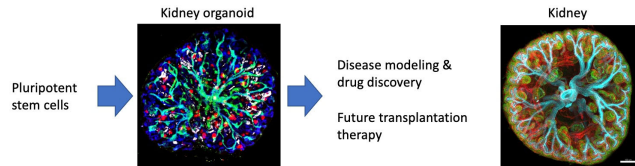


Figure 1 : Generation and application of kidney organoids

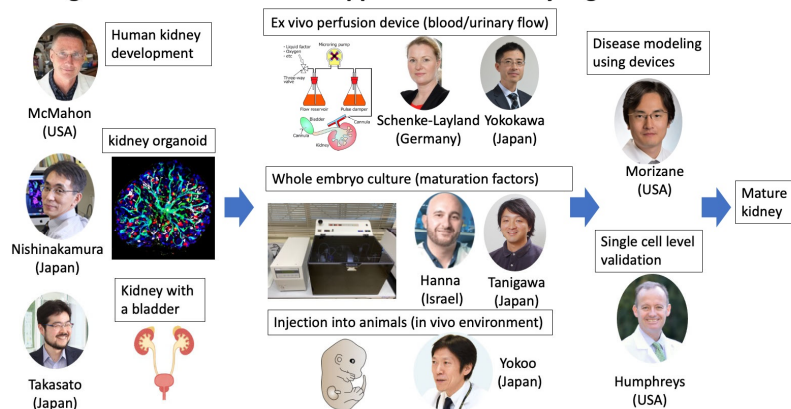


Figure 2. Creating a mature human kidney

### Organization of the Project Team

#### ● International network of 10 leading researchers

This project aims to produce next-generation kidney organoids and functional maturity (Figure 2, 3). **McMahon (USA)** investigates the human kidney development and provide the information to **Nishinakamura (Japan)**, who will generate the human kidney organoid with higher-order structure. **Takasato (Japan)** will generate bladder organoids and establish a method to connect bladder and kidney organoids, together with Nishinakamura. The resultant organoids will be provided to **Yokokawa (Japan)** and **Schenke-Layland (Germany)**, both of who will develop ex vivo perfusion devices, in which the organoids are perfused via vasculature and produce urine in vitro. **Morizane (USA)** will use these functional organoids in devices to reproduce diseases with advanced accuracy. **Tanigawa (Japan)** will search for maturation factors and collaborate with **Hanna (Israel)**, who has developed the revolutionary ex utero whole embryo culture system. They will add candidate maturation factors to the culture for verification, which will then be applied to the kidney organoids in perfusion devices to further mature the organoids. **Yokoo (Japan)** will transplant the human kidney organoids into animals to allow them to mature in vivo. **Humphreys (USA)** will analyze the generated organoids at the single cell level and provide feedback to improve the quality and maturity of the organoids.

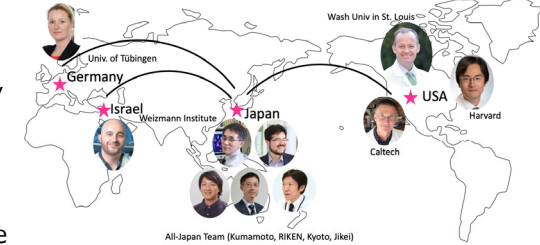


Figure 3. Global network to generate transplantable kidney organoids

### Plan for Fostering Early-career Researchers

#### ● A talent development system that transcends laboratory and national boundaries

We will continuously train young researchers who will lead the science and industry based on the following plan (Figure 4). Six postdoctoral fellows will be hired, 3 of whom will be sent overseas at any given time. Eleven graduate students will be hired as Research Assistants, half of whom will be sent abroad for short term. A total of 17 people will be hired, and travel expenses to attend international research conferences will be supported. At monthly web meetings, young scientists will present their research, and all principal investigators will give advice. Graduate students and postdoctoral fellows who are currently sent overseas will be invited to participate in these meetings to develop the next group of postdocs overseas. We will hold an in-person retreat/international symposium at Mt. Aso in Kumamoto every year to promote the scientific and social interactions. We will also organize a seminar series on entrepreneurship to provide diverse career paths for young researchers. Finally, core facilities at Kumamoto University, RIKEN, and Kyoto University will be opened to the members of this project to promote the growth and independence of young researchers.

- 6 postdocs & 11 graduate students
  - Monthly web meeting & feedback
  - Annual retreat at Mt. Aso, Kumamoto
  - Independent research funds and start-up funds
  - Travel expense assistance
  - Gender bias improvement
  - Entrepreneurship Seminar Series
- Helping young people grow by using Core Facilities



Figure 4. Global environment to support young scientists