October 14, 14:00- 15:00 Plenary Lecture

Recent Progress in iPS Cell Research and Application

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Induced pluripotent stem cells (iPSCs) can proliferate almost indefinitely and differentiate into multiple lineages, giving them wide medical applications. As a result, they are being used for new cell-based therapies, disease models, and drug development around the world.

In our basic research, we are focusing on the mechanisms of protein translational regulation in the proliferation and differentiation of iPSCs. We have previously reported that the translation regulator NAT1 is essential for the self-renewal and neuronal differentiation potential of hiPSCs, which is a "Bench to Bedside" activity for the medical application of iPSCs.

As translational research, we are proceeding with an iPSC stock project in which clinical-grade iPSC clones are being established from healthy donors with homologous HLA haplotypes to lower the risk of transplant rejection. We started distributing the iPSC stock to domestic and overseas institutions, and related clinical studies have begun for age-related macular degeneration (AMD), Parkinson's disease, corneal epithelial stem cell deficiency, and other diseases, giving expectation that iPSC-based regenerative medicine will be widely used in the future. However, donors with HLA homozygous are rare. Genome editing technology could be used to reduce the transplant-rejection risk. Indeed, we reported HLA gene-edited iPSCs that could expand the range of patients who benefit from iPSC therapies faster than the homologous HLA haplotype strategy. This technology also has the potential to prevent or treat genetic diseases and gives great hope to patients.

Other applications of iPSCs are drug screening, toxicity studies, and disease modeling. In 2017, a new drug screening system using iPS cells for fibrodysplasia ossificans progressiva (FOP) was reported, revealing one drug candidate, Rapamycin, which is now undergoing a clinical trial to treat FOP patients. Additionally, Bosutinib, a drug for leukemia was revealed to be efficacious for amyotrophic lateral sclerosis (ALS) using a disease-specific iPSC model. Accordingly, we initiated a Phase 1 clinical trial of Bosutinib to treat ALS at Kyoto University Hospital and other centers in 2019 and began Phase 2 clinical trials in April 2022. Furthermore, we initiated a Phase I clinical trial of Bromocriptine to treat Alzheimer's disease at Kyoto University Hospital in June 2020. Thus, drug repurposing using iPS cells is progressing at an accelerated pace.

Over the past decade, iPSC research has made great progress, moving toward innovative therapeutics for people with intractable diseases by the application of new findings from basic science and reverse translation from clinics.