Division of Regenerative Medicine

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General Summary

Regenerative medicine is rapidly moving toward translation to clinical medicine. However, a better understanding of the molecular pathways leading to human diseases is required for regenerative medicine to succeed. Good animal models will play a key role in research to increase our understanding of the diseases. Disease models in genetically engineered mice are extremely useful but do not always precisely recapitulate the pathophysiology of human disease, especially disorders of the central nervous system. We have recently attempted to create a transgenic primate model of human neurodegenerative diseases through forced expression of dominant mutant genes. On the other hand, induced pluripotent stem (iPS) cell technology has given us the ability to generate and expand various types of differentiated cell from patient-derived cells; iPS cells are now being applied to cell therapy and being used to study of the mechanisms of disease. Advances in disease modeling with patient-derived cells and nonhuman primates will have an enormous affect on future opportunities and advances in biomedical research.

Research Activities

Therapeutic strategies for the damaged central nervous system

Recent advances in developmental and stem-cell biology have made regeneration-based therapies feasible for patients with damaged central nervous systems, including those with spinal cord injuries, Parkinson's disease, or stroke. Understanding and then controlling the appropriate regulatory mechanisms in neural stem cells (NSCs) will be important milestones in the development of regeneration-based treatments for damaged central nervous system tissue. Previously, we observed how transplanted iPS cell–derived NSCs were integrated in the injured spinal cord and differentiated into various kinds of cell, including neurons, astrocytes, and oligodendrocytes. Although the precise mechanism of symptomatic improvement remains unclear, NSC transplantation has promoted functional recovery in experimental studies in rats and nonhuman primates.

In-vivo imaging technology applied to regenerative medicine

Bioluminescence imaging is an efficient and powerful method for longitudinal comparison of cell survival and migration. Cell therapies can be more quickly optimized and refined with imaging, which is widely applicable to various types of regenerative medicine, including stem-cell therapies. We used *in-vivo* bioluminescence imaging to noninvasively assess the survival and residence time of transplanted NSCs at injury sites in living animals. Photon signals from these cells were detectable through normal tissues, such as bone and skin, with ultrasensitive cooled charged–coupled device cameras for 10

months or more after transplantation into the injured spinal cords of mice.

Common marmoset as a primate disease model

The common marmoset (*Callithrix jacchus*) is becoming an increasingly popular primate animal model in biomedical research, because of its advantage of translation to genetically similar human systems. Marmosets, because of their small size and high reproductive rate, are suitable subjects for transgenic modification. Recently, transgenic marmosets were successfully created by gene transduction into embryos; this animal model is genetically similar to humans and can be used to study human neurodegenerative diseases, such as Parkinson's disease and amyotrophic lateral sclerosis. Good animal models will play a key role in research to increase our understanding of the pathophysiology of neurodegenerative diseases. We have recently attempted to create a transgenic marmoset model of human neurodegenerative diseases through forced expression of dominant mutant genes.

Publications

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