Department of Genetic Diseases and Genome Science

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General Summary

The main research topics in the Department of Genetic Diseases and Genome Science are the basic pathogenesis of genetic diseases, particularly, lysosomal storage diseases (LSDs), and the development of therapies for LSDs. Of our research topics, the pathogenesis of central nervous system (CNS) involvement in LSDs is the most important. To understand the pathophysiology of CNS events in LSDs, we generated induced pluripotent stem (iPS) cells from mucopolysaccharidosis (MPS) VII mice and caused them to differentiate into neuronal cells. We also generated iPS cells from a mouse model of Pompe disease and caused them to differentiate into skeletal muscle cells. We can produce disease models of various LSDs using iPS technology. Furthermore, we treated CNS involvement of LSDs by means of intrathecal injection of enzymes into MPS II mice. These findings indicate that intrathecal treatment is feasible for treating the CNS in various LSDs.

Research Activities

1. iPS cells from various LSDs are important research tools for understanding the pathophysiology of LSDs and can also be applied to the treatment of LSDs. We successfully generated iPS cells from Pompe mice by means of tail-tip fibroblasts, mouse embryonic fibroblasts, and 3 factors: Klf4, Sox2, and Oc2/4t. The iPS cells differentiated into skeletal muscle cells. Pompe skeletal muscle cells showed massive accumulation of glycogen in lysosomes surrounded by a single membrane unit. We also generated iPS cells from patients with Gaucher disease, Fabry disease, and Pompe disease.
2. Development of treatment procedures for LSDs
To establish novel treatment procedures for CNS involvement of LSDs is our most important project. One procedure is intrathecal or intraparenchymal injection of enzymes into MPS II mice. We found that intrathecal injection produced significant elevations of enzyme activities in various regions of the brain and in other organs, such as the liver, spleen, kidney, and heart. Furthermore, histological improvement in the brains of MPS II mice was also observed.
3. The screening for LSDs with dried blood spots is an important technology for the early diagnosis and treatment of patients with various LSDs. We used the fluorometric assay method to establish the dried blood spot method for the early diagnosis of Pompe disease, Fabry disease, Morquio syndrome, and MPS VI. Furthermore, we recently established a dried blood spot diagnostic method for Wolman disease.

Publications

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