Department of Genetic Disease Research (Lysosomal Storage Disease)

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General Summary

The Donated Department of Genetics and Genome Science was established on April 1, 2008. The main topic studied is the basic pathogenesis of genetic diseases, particularly, lysosomal storage diseases (LSDs). In particular, the pathogenesis of central nervous system (CNS) involvement in LSDs is the most important problem. To understand pathophysiology of the CNS events, we have generated induced pluripotent stem cells (iPSCs) from mucopolysaccharidosis (MPS) VII mice and caused them to differentiate into neuronal cells. We also generated iPSCs from model mice of Fabry disease and Pompe disease and caused them to differentiate into cardiac cells and skeletal muscle cells. Furthermore, we attempted to treat CNS involvement of LSDs by intrathecal injection of enzymes into MPS II mice. The promising results suggest that lysosomal storage in neuronal cells can be treated in MPS II mice.

Research Activities

1. To establish novel treatments for CNS involvement is an intriguing problem; such treatments include the intrathecal or intraparenchymal injection of enzyme into MPS II mice. We also performed gene therapy of Pompe disease by means of a lentivirus vector. Sufficient expression of the alpha-glucosidase gene was observed in cardiac muscle, but expression was less in skeletal muscle.
2. To establish new technologies of iPSCs from various LSDs for understanding the pathophysiology of LSDs and developing new therapies, we successfully isolated iPSCs from skin fibroblasts of twitcher, Fabry, and Sly mice and caused them to differentiate into many cell types. Four factors were used — hKlf4, hSox2, hc-Myc, and hOct — and Myc was also deleted to isolate iPSCs (Mao, Shen, Ohashi, Eto, 2009). We also recently established the iPSCs from human Pompe disease and caused them to differentiate into skeletal muscle cells.
3. We evaluated the efficacy of enzyme replacement therapy in terms of serum antibody titers in patients with Fabry disease and Pompe disease. Results indicated that high antibody titers in serum inhibited enzyme uptake and neutralized activities. These results indicate that high serum antibody titers against enzymes influence the efficacy of enzyme administration for patients with Fabry disease and Pompe disease.

4. To establish new screening procedures for LSDs with dried blood spots is an important technology for the early diagnosis and treatment of patients with Pompe disease and Fabry diseases. We established the dried blood spot method for the early diagnosis of Pompe disease and Fabry disease and other LSDs using 4-methylumberyferon derivatives.

Publications

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Presentations

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