Develop personalized cell-based therapy for myotonic dystrophy type 1 using genome-edited iPS cells

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Abstract

Myotonic Dystrophy 1 (DM1) is the most common adult form of muscular dystrophy caused by expanded CTG repeat in 3' UTR. No treatment is presently available for DM1. With the advancement of iPS cell ((iPSC) technologies, there has been increasing enthusiasm about applying iPS technology to generate autologous cells for therapeutic purpose. However, the major hurdle in the therapeutic application of iPSC in genetic disorders is that patient-derived cells still carry the gene. The ideal solution is to correct the mutation prior to transplantation to prevent DM1 stem cells and their progeny from undergoing the same degenerative process after transplantation. We have developed a strategy to completely eliminate expanded CUG mutant transcripts using CRISPR/Cas9 technology. The genome-corrected DM1 iPSC as well as the linearly differentiated skeletal myogenic precursor cells (SMPC) demonstrated loss of intranuclear RNA foci. These genome-corrected SMPC can be further differentiated into myotube and mature myofibers comparable to normal iPSC-derived SMPC. In comparison, parental DM1 iPSC-derived SMPCs have poor myotube formation and early degeneration of myofibers. We conclude therapeutic genome editing of DM1 iPSC is an applicable approach to generate healthy SMPCs for autologous stem cell transplantation therapy.

Biography

Guangbin Xia, MD, PhD. is an associate professor in Department of Neurology and Neuroscience of University of New Mexico. Dr. Xia got his MD degree in Shanghai, China and his PhD degree in Tokyo, Japan. He had further scientific training as a postdoctoral fellow at the University of Southern California. Subsequently, he had his Medicine Internship training in the University of Virginia and Neurology Residency training in University of Texas Medical Branch and University of Florida. Dr. Xia also received his Master's degree in Clinical and Translational Science. He started his research on neurodegenerative disorders since his residency training when he was at the University of Texas Medical Branch. After he completed his residency and fellowship training in University of Florida, he began to focus his research on induced pluripotent stem (iPS) cell for neurodegenerative disorder. He has established iPS cell lines for myotonic dystrophy, spinocerebellar ataxia, and ALS. He has recently moved to University of New Mexico. His lab locates in a prestigious facility (FACE, facility for advanced cell engineering). He is using these disease-specific iPS cells lines for therapeutic development, including therapeutic genome editing on iPS cells for cell-based therapy and *in vivo* genome editing.