

Center for Gene & Cell Therapy

遺伝子・細胞治療センター

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IMSUT hospital has been playing a lead role in gene therapy and hematopoietic stem cell transplantation in Japan. In order to strengthen this clinical development even further, IMSUT established the Center for Gene & Cell Therapy (CGCT) in 2014. CGCT particularly focuses on the development of gene therapy and cell therapy for intractable cancer and chronic diseases such as oncolytic virus therapy, engineered T cell therapy, gene therapy for neurological disorders using AAV vectors, T cell therapy for post-transplant viral infections, and cell therapy using mesenchymal stem cells.

1. Gene therapy for amyotrophic lateral sclerosis and spinocerebellar ataxia type 6

Shin-ichi Muramatsu, Sumimasa Nagai and Keiya Ozawa

In sporadic amyotrophic lateral sclerosis (ALS) patients, down regulation of the RNA-editing enzyme, adenosine deaminase acting on RNA 2 (ADAR2), is death-causing molecular abnormality

that occurs in motor neurons. Gene delivery of the ADAR2 using adeno-associated virus (AAV) vectors in conditional ADAR2 knockout mice effectively prevented progressive motor dysfunction without any adverse effects. We have started to produce GMP grade AAV vectors that express ADAR2 for a clinical trial. In collaboration with Chicago university, we have developed miR-based gene therapy for spinocerebellar ataxia type 6 (SCA6). SCA6 is caused by abnormal expansions of

the polyglutamine tract within a second *CACNA1A* gene product, α 1ACT. Selective translational block of SCA6-associated α 1ACT by delivering miR-3191-

5p protected from the Purkinje cell degeneration and ataxia in a mouse model.

Publications

1. Miyazaki, Y., Du, X., Muramatsu, S. and Gomez, C.M. A miRNA-mediated therapy for SCA6 blocks IRES-driven translation of the *CACNA1A* second cistron. *Sci Transl Med*, 8(347): 347ra94, 2016.
2. Kanazawa, M., Ohba, H., Harada, N., Kakiuchi, T., Muramatsu, S. and Tsukada, H. Evaluation of 6-¹¹C-methyl-*m*-tyrosine as a PET probe for pre-synaptic dopaminergic activity: a comparison PET study with β -¹¹C-L-DOPA and ¹⁸F-FDOPA in Parkinson's disease monkeys. *J. Nucl. Med.* 57(2): 303-308, 2016.
3. Igarashi, H., Koizumi, K., Kaneko, R., Ikeda, K., Egawa, R., Yanagawa, Y., Muramatsu, S., Onimaru, H., Ishizuka, T. and Yawo, H. A Novel Reporter Rat Strain That Conditionally Expresses the Bright Red Fluorescent Protein tdTomato. *PLoS One*, 11(5): e 0155687, 2016.
4. Ono, S., Sato, T. and Muramatsu, S. Freezing of gait in Parkinson's disease is associated with reduced 6-[¹⁸F]fluoro-*l*-*m*-tyrosine uptake in the locus coeruleus. *Parkinsons Dis*, 2016: Article ID 5430920, 5 pages, 2016.
5. Higashida, H., Yokoyama, S., Tsuji, C. and Muramatsu, S. Neurotransmitter release: vacuolar ATPase V0 sector c-subunits in possible gene or cell therapies for Parkinson's, Alzheimer's, and psychiatric diseases. *J Physiol Sci*, *in press*.