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Transgenic technique to 'eliminate' a specific neural circuit of the brain in primates

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Japanese researchers developed a gene transfer technique that can "eliminate" a specific neural circuit in non-human primates for the first time in the world.

In the brains of humans and non-human primates, over 100 billion nerve cells build up complicated neural circuits and produce higher brain functions. When an attempt is made to perform gene therapy for neurological diseases like Parkinson's disease, it is necessary to specify a responsible neural circuit out of many complicated circuits. Until now, however, it was difficult to introduce a target gene into this particular circuit selectively. The collaborative research group consisting of Professor Masahiko TAKADA from Primate Research Institute, Kyoto University, Professor Atsushi NAMBU from National Institute for Physiological Sciences, National Institutes of Natural Sciences, and Professor Kazuto KOBAYASHI from Fukushima Medical University School of Medicine succeeded in development of the gene transfer technique that can "eliminate"a specific neural circuit in non-human primates for the first time in the world .

They applied this technique to the basal ganglia, the brain region that is affected in movement disorders such as Parkinson's disease, and successfully eliminated a particular circuit selectively to elucidate its functional role. This technique can be applied to gene therapy for various neurological diseases in humans. This research achievement was supported by the Strategic Research Program of Brain Sciences by MEXT of Japan, and published in the American science magazine *PLoS*

ONE (June 25th issue electronic edition).

The research group developed a special viral vector, NeuRet-IL-2R alpha-GFP viral vector, expressing human interleukin type 2 alpha receptor, which the cell death inducer immunotoxin binds. Nerve cells transfected with this viral vector cause cell death by immunotoxin. First, the research group injected the viral vector into the subthalamic nucleus that is a component of the basal ganglia. Then, they injected immunotoxin into the motor cortex, an area of the cerebral cortex that controls movement, and succeed in selective elimination of the "hyperdirect pathway" that is one of the major circuits connecting the motor cortex to the basal ganglia. As a result, they have discovered that neuronal excitation observed at the early stage occurs through this hyperdirect pathway when motor information derived from the cortex enters the basal ganglia.

Professors TAKADA and NAMBU expect that this gene transfer technique enables us to elucidate higher brain functions in primates and to develop primate models of various psychiatric/neurological disorders and their potential treatments including gene therapy. They think that this should provide novel advances in the field of neuroscience research that originate from Japan.

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