THE I2020T LRRK2-EXPRESSING TRANSGENIC MOUSE EXHIBITS IMPAIRED LOCOMOTIVE ABILITY

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Introduction: Leucine-rich repeat kinase (LRRK2) is the gene responsible for autosomal dominant Parkinson's disease (PD), PARK8. The patients of the original PARK8 family (Sagamihara family) have the I2020T mutation in the kinase domain of LRRK2, but the mechanism responsible for neurodegeneration remains undisclosed.

Aim: To establish a mouse model of PD caused by I2020T LRRK2, we created a transgenic mouse line.

Methods: The human I2020T LRRK2 cDNA had been expressed in C57BL/6 mice under the control of the CMV promoter. The transgenic mice aged 13 months and their normal littermates were subjected to the rotarod learning test, beam test, and cylinder test for examination of motor ability, to the hidden prey test for olfactory examination, and to the open field test for behavioral examination.

Results: Immunohistochemical analysis of the brain revealed that dopamine neurons as well as other neurons expressed the mutant LRRK2. In both the rotarod test and beam test, the transgenic mice exhibited impaired locomotive ability, whereas in the cylinder test the frequency of leaning was rather higher in the transgenic mice than in the littermates. The transgenic mice behaved normally in the open field test and exhibited a normal sense of smell in the hidden prey test. No decrease of dopamine neurons has been detected so far up to the age of 19 months. We are now examining the biochemical abnormality from various aspects.

Conclusion: We have established a transgenic mouse line expressing I2020T mutant LRRK2, which exhibits impaired locomotive ability.