

Researchers develop first transgenic nonhuman primate model of Huntington's disease

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In the first study of its kind, researchers at the Yerkes National Primate Research Center, Emory University, in collaboration with researchers from the Department of Human Genetics at Emory's School of Medicine, have developed the first transgenic nonhuman primate model of Huntington's disease (HD), one of the most devastating human neurodegenerative diseases.

This development, reported in the May 18 Advance Online Publication of *Nature*, is expected to lead to greater understanding of the underlying biology of HD and to the development of potential therapies. In addition, this pioneering study, which was supported by a grant from the National Institutes of Health, is leading the way toward the development of nonhuman primate models of other genetic diseases.

HD is a genetic, neurodegenerative disorder that causes uncontrolled movements, loss of mental processing capabilities and emotional disturbances. Patients succumb to the disease within 10 to 15 years of the onset of the symptoms.

According to lead researcher Anthony W.S. Chan, DVM, PhD, "In the past, researchers have used transgenic mouse models to study the disease. These models do not completely parallel the brain changes and behavioral features observed in humans with HD, thus making the development of a transgenic nonhuman primate model critical to

currently treating and ultimately preventing the disease."

Chan, an assistant research professor at the Yerkes Research Center and an assistant professor in the Department of Human Genetics, and his research team (Yerkes: J. Bachevalier, Y. Smith, S. Zola; and Department of Human Genetics: SH Li, XJ Li), produced the HD transgenic rhesus macaques by:

-- Injecting 130 mature oocytes with:

* a lentivirus expressing the mutant htt gene with expanded polyglutamine

repeats, which is the primary cause of HD, and

* a lentivirus expressing a green fluorescent protein (GFP) gene;

-- Fertilizing the oocytes by intracytoplasmic sperm injection (ICSI); and

* Transferring 30 embryos into eight surrogates.

* This resulted in six pregnancies and five live births (two sets of twins and one singleton); all carried the mutant htt and GFP genes. Two continue to survive.

Chan noted, "The transgenic monkeys are providing us with unparalleled opportunities for behavioral and cognitive assessments that mirror the assessments used with humans. With such information, much of which we are obtaining by using the Yerkes Research Center's extensive imaging capabilities, we are developing a more comprehensive view of the disease than currently available."

Chan's research team is one of several at Yerkes focused on the genetic basis of neurodegenerative diseases, including Alzheimer's and Parkinson's diseases.

"This study is a complement to the many neuroscience programs at Yerkes and further solidifies our role at the forefront of neuroscience

research," said Stuart Zola, PhD, director of the Yerkes Research Center and the study's co-investigator leading the behavioral assessments.

"Access to Emory's department of human genetics, our collaborations with the department of neurology, our own imaging center and, of course, our animal colony make Yerkes one of the few places in the world where this type of study can be done," Zola continued.

The researchers, who are continuing to monitor and assess the transgenic monkeys, believe their progress bodes well for developing transgenic nonhuman primate models of other neurodegenerative diseases, such as Alzheimer's. "The development of all such models is invaluable for understanding disease pathogenesis and for developing early diagnostic and treatment strategies," Zola continued.

For more than seven decades, the Yerkes National Primate Research Center, Emory University, has been dedicated to conducting essential basic science and translational research to advance scientific understanding and to improve the health and well-being of humans and nonhuman primates. Today, the center, as one of only eight National Institutes of Health funded national primate research centers, provides leadership, training and resources to foster scientific creativity, collaboration and discoveries. Yerkes-based research is grounded in scientific integrity, expert knowledge, respect for colleagues, an open exchange of ideas and compassionate, quality animal care.

Source: Emory University

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