

A new kind of rat model

September 13 2007

Two neuroscientists at the University of Wisconsin-Milwaukee (UWM) are working with local company PhysioGenix to investigate a novel animal model the company has developed for researching diseases like depression, anxiety, schizophrenia and ADHD.

The models are genetically altered rats, originally created by researchers at the Medical College of Wisconsin (MCW) as a way to clone genes related to human diseases. Called consomic rats, they were produced by replacing a single chromosome from the genetic background of a “diseased” rat with the same chromosome from a “normal” rat.

In theory, if the new strain is “cured” of a disease, then the genes responsible for the disease are either on the transferred chromosome or somehow related to it. Consomic rats can be used to rapidly identify new genes and cellular targets associated with certain diseases and to develop and test the efficacy of new drug therapies.

In fact, the consomic rats have already proved useful in studies of cardiovascular disease and hypertension – the main reason for their development.

The process of identifying which genes are the players in certain complex diseases or behaviors is much quicker using consomic rats than by traditional gene-hunting methods, says Steven Nye, director of genomics at PhysioGenix and principal investigator of the National Institutes of Health grant for commercializing the consomic rats.

PhysioGenix, a spin-off company founded by researchers at MCW, has contracted with UWM Psychology Professors Rodney Swain and Fred Helmstetter to characterize the rats' behaviors in a battery of psychological tests to confirm whether chromosome substitution improves their conditions.

The task is daunting, considering there are 44 strains of consomic rats and potentially hundreds of psychological tests to choose from.

Currently, Swain and Helmstetter are probing their efficacy in identifying the genetic roots of psychological disorders related to learning and memory. Insights from the research could lead to a wide spectrum of related research, he says.

"The impairments that we saw in one consomic strain are similar to some of the symptoms that you see in human children with autism or attention deficit hyperactivity disorder (ADHD)," Swain says.

Test results so far have shown that some of the consomic rats exhibited increased depressive-like behavior, increased pain sensitivity, lower expression of anxiety and enhanced learning in spatial navigation tasks.

The researchers say their findings illustrate the role of genetics on behavior.

"Since my lab has been studying how angiogenesis (the creation of new blood vessels) contributes to better learning, we were very interested to see how this consomic strain performed on a variety of learning tasks," he says.

PhysioGenix, which opened its lab six years ago, licensed the intellectual property from MCW that allows it to commercialize the consomic rats, and the company is finding new applications for them. Howard Jacob,

one of the founders of PhysioGenix, is also director of the Human Molecular Genetics Center at MCW. He was instrumental in creating the consomic rats, and was a leader in the rat genome sequencing project funded through the National Institutes of Health. Richard Roman, director of the Kidney Disease Institute at MCW, also is a co-founder of PhysioGenix.

Together, researchers at PhysioGenix, along with their UWM partners, will be presenting three papers at the annual meeting of the Society for Neuroscience in November.

Ultimately, PhysioGenix plans to distribute the consomic rats to academic researchers for studying human neurological diseases and to pharmaceutical researchers for developing new drug therapies.

Source: University of Wisconsin - Milwaukee

Citation: A new kind of rat model (2007, September 13) retrieved 24 May 2024 from <https://medicalxpress.com/news/2007-09-kind-rat.html>

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