



Mini-Mouse Is a Bad Mom

October 15, 2004

Female mice that are abnormally small due to gene “knockout” technology are also bad mothers whose poor parenting skills cause their young to die within a day or two of birth, scientists report this week in the on-line edition of the *Proceedings of the National Academy of Sciences*.

Since Chawnsang Chang, Ph.D., cloned the gene for testicular orphan receptor 4 (TR4) 10 years ago, he and other scientists have tried to learn its function – scientists call it an “orphan” receptor because they don’t know what protein links up with it. So a team led by Chang, director of George Whipple Laboratory for Cancer Research at the University of Rochester Medical Center, knocked out the gene in mice, then watched what happened.

They found that many of the mice died before birth. Those that lived are markedly smaller than their normal counterparts: They’re born far smaller and then make up some of the difference as they grow, but generally they are about 20 to 30 percent smaller by the time they reach adulthood. The miniature mice are not as fertile as normal mice, having only about half the offspring as other mice.

Most visibly, the females have very bad parenting skills: They don’t build nests, nurse their young, or tend to their offspring, which die within a day or two as a result.

“Basically, we observed mothers that don’t care for their pups,” says post-doctoral associate Loretta Collins, Ph.D., who did much of the work along with Yi-Fen Lee, Ph.D., assistant professor of urology. “A normal mouse will gather its offspring and crouch over them and take care of them, but these “knockout” mice just left their pups scattered about the cage.

“Our plans to further characterize behavior and gene expression in these animals will help us identify the target genes that are normally controlled by TR4 and contribute to regulation of specific behaviors,” she adds.

Scientists have known that the receptor is present throughout tissues such as muscle, spleen, thyroid gland, the testes, and the cerebellum, but they didn’t expect that knocking out the receptor would have such broad effects.

“TR4 is a master regulator that binds to other genes and turns on or blocks other genes,” Chang says. “Now we know that it plays an important role in growth, development, and reproduction as well.”

In addition to Chang, Collins, and Lee, other authors from Rochester include Cynthia A. Heinlein, Ning-Chun Liu, Yei-Tsung Chen, and Chih-Rong Shyr. The team also included Charles K. Meshul of the Oregon Health and Science University, Hideo Uno of the University of Wisconsin, and Kenneth A. Platt from Lexicon Genetics Inc. of Texas.

The work was funded by the National Institute of Diabetes and Digestive and Kidney Diseases.

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Tom Rickey | Source: EurekAlert!

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