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### **It's in the genes: Study opens door to new treatment of the blues**

A Florida State University scientist used a gene transfer technique to block the expression of a gene associated with clinical depression in a new study of mice that could lead to better treatment of human beings with this condition.

Carlos Bolanos, an assistant professor of psychology and neuroscience, was among a team of researchers that identified the role of a gene called Brain Derived Neurotrophic Factor (BDNF) in the development of social aversion. Mice treated with a transfer technique to block expression of the BDNF gene in a small area of the mid-brain did not develop the aversion despite repeated encounters with aggressive rodents. The study will be published in the Feb. 10 issue of the journal *Science*.

"It's very exciting because we are slowly but surely identifying mechanisms in the brain underlying psychiatric disorders that have a social withdrawal component, such as social phobia, depression and post-traumatic stress disorder, and that will allow us to find better ways to treat these disorders," Bolanos said. "This study is significant because it gives us an animal model of the disorder and opens up new areas of study."

In the experiment, the researchers subjected mice to daily bouts of social threats and subordination by aggressive rodents and continuous sensory contact with the aggressors for 10 days. Afterward, the defeated mice avoided any social contact by spending most of their time in the corner of their cages opposite other mice, including those that had not been aggressive toward them.

The defeated mice also displayed little interest in sexual interaction and showed decreased preference for palatable sugary drinks over plain water. A month later, the rodents' interest in sex and sweets had returned, but the social avoidance remained.

The researchers found that long-term use of antidepressants, such as fluoxetine (Prozac) and imipramine (Tofranil), were successful in reversing the social withdrawal in these mice. But the successful use of the gene therapy approach to block the

expression of the BDNF gene in a highly localized area of the brain suggests the potential for the development of new drug therapies with fewer side effects.

"We have made great progress in our understanding of how antidepressants work, but despite years of research, our knowledge of the changes that these drugs induce in the brain is rudimentary," Bolanos said. "Though available treatments for depression are generally safe and effective, they are still not ideal. It takes long-term treatment before seeing clinical benefit, and potential side effects are a serious problem. The findings of this study provide exciting new leads and point to potential strategies, such as developing drugs capable of targeting specific proteins in restricted brain areas."

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