

FOR IMMEDIATE RELEASE
Wednesday, May 13, 2009

NIDA Contacts: Stephanie Older
301-443-6245
media@nida.nih.gov

NIDA Study Reveals Widespread Effects of Cocaine on Genome Structure and Function
Scientists see vast clinical potential of newly identified gene targets

Repeated use of addictive drugs such as cocaine causes long-lasting changes in parts of the brain involved in motivation and reward, among others, yet the precise mechanisms by which these changes are maintained are poorly understood. A new study by scientists supported by the National Institute on Drug Abuse (NIDA), published May 14, 2009 in the journal *Neuron*, sheds light on this process by providing fundamental new insights into the effects of cocaine on the structure and function of the genome, the complete set of DNA instructions needed to make an organism.

“This study’s findings enable us to glimpse for the first time exactly how cocaine modifies the activity of genes in regions of the brain that mediate reward,” says NIDA Director Dr. Nora Volkow. “In addition, this research has identified a novel family of genes that appear to play a key role in the brain’s response to cocaine. These genes represent promising new targets for the development of medications to treat cocaine addiction.”

Investigators led by Eric Nestler, M.D., Ph.D., of Mount Sinai School of Medicine in New York, used a powerful new molecular analysis technique, known as ChIP-chip, to observe changes in gene activity in the brains of laboratory mice injected with cocaine. These changes involve alterations in proteins called histones and transcription factors, which bind to DNA and regulate the process by which the genetic information in a strand of DNA is read in order to generate a complementary sequence of RNA. Translation machinery within the cell then uses the information in the RNA sequence to manufacture the final protein products.

“Using these markers of gene activity, we mapped the genomic effects of chronic cocaine use in the nucleus accumbens, which is a key component of the brain’s reward circuitry,” explains Dr. Nestler. “This analysis provides fundamentally new information about the range of genes that are altered by cocaine in this brain region. For example, this study demonstrated, for the first time, that a family of genes called the sirtuins are activated in the nucleus accumbens by chronic

cocaine administration and contribute to addiction-related behaviors in animal models.

“We showed that blocking the activity of the sirtuins specifically in the nucleus accumbens reduced both cocaine’s rewarding effects and the motivation to self-administer the drug,” said Dr. Nestler. These findings raise the possibility of using sirtuin inhibitors as treatment agents for cocaine addiction. Further analysis of other genes activated and inhibited by cocaine may help to identify additional therapeutic targets for addiction treatment.

Dr. Nestler led the study in collaboration with colleagues at the University of Texas Southwestern Medical Center at Dallas and Florida State University in Tallahassee.

###

The National Institute on Drug Abuse is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world’s research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to inform policy and improve practice. Fact sheets on the health effects of drugs of abuse and information on NIDA research and other activities can be found on the NIDA home page at www.drugabuse.gov. To order publications in English or Spanish, call NIDA’s new DrugPubs research dissemination center at 1-877-NIDA-NIH or 240-645-0228 (TDD) or fax or email requests to 240-645-0227 or drugpubs@nida.nih.gov. Online ordering is available at <http://drugpubs.drugabuse.gov>.

The National Institutes of Health (NIH) — *The Nation's Medical Research Agency* — includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary Federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases. For more information about NIH and its programs, visit www.nih.gov.