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Enzyme might be target for treating smoking, alcoholism at same time

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An enzyme that appears to play a role in controlling the brain's response to nicotine and alcohol in mice might be a promising target for a drug that simultaneously would treat nicotine addiction and alcohol abuse in people, according to a study by researchers at the Ernest Gallo Clinic and Research Center, affiliated with the University of California, San Francisco.

Over the course of four weeks, mice genetically engineered to lack the gene for protein kinase C (PKC) epsilon consumed less of a nicotine-containing water solution than normal mice, and were less likely to return to a chamber in which they had been given nicotine.

In contrast, normal mice steadily increased their consumption of nicotine solution while the mice lacking PKC epsilon did not.

The study was conducted by Gallo senior associate director and investigator Robert O. Messing, MD, UCSF professor of neurology, and Gallo researcher Anna M. Lee, PhD.

In normal mice, as in humans, nicotine binds to a certain class of nicotinic receptors located on dopamine neurons, which causes dopamine to be released in the brain. Dopamine creates a feeling of enjoyment, and thus prompts a sense of reward. Lee and Messing found that mice lacking PKC epsilon are deficient in these nicotinic receptors.

The study appears in the online Early Edition of the Proceedings of the

National Academy of Sciences for the week of September 12, 2011.

The finding complements earlier research in which Messing found that mice genetically engineered to lack the PKC epsilon enzyme drank less alcohol than normal mice and were disinclined to return to a chamber in which they had been given alcohol.

"This could mean that these mice might not get the same sense of reward from nicotine or alcohol," said Messing. "The enzyme looks like it regulates the part of the reward system that involves these nicotinic receptors." The reward system is a complex of areas in the brain that affect craving for nicotine, alcohol and other addictive substances.

The next step in the research, said Messing, would be to develop compounds that inhibit PKC epsilon. The ultimate goal, he said, would be medications that could be used "to take the edge off of addiction by helping people get over some of their reward craving."

More information: "Protein kinase C epsilon modulates nicotine consumption and dopamine reward signals in the nucleus accumbens," by Anna M. Lee and Robert O. Messing, *PNAS*.

Provided by University of California, San Francisco