

## Brown Deer High School SMART Team

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### NMDAR Helps You Think, So Please Reconsider That Extra Drink

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According to the U.S. Centers for Disease Control and Prevention, each year 88,000 people die from alcohol-related causes in the United States. Ethanol misuse, a deadly and expensive societal problem, cost the United States \$249 billion in 2010 (1). Ethanol targets many proteins in the brain. Specifically, it acts as an inhibitor of the N-Methyl-D-aspartate receptor (NMDAR), which mediates much of the excitatory synaptic transmission in the brain. Normally, the NMDAR is activated when glutamic acid binds to it allowing positive ions to flow through the cell membrane; this facilitates learning and memory in the brain. However, ethanol inhibits the activity of the NMDAR, interfering with synaptic transmission. A type of glutamate ion channel receptor found in neurons, NMDAR, has four domains: the amino terminal domain, the ligand binding domain, the membrane-associated (M) domains, and the carboxy terminal domain. NMDAR is a heterotetrameric protein with two GluN1 and two GluN2 subunits. Ethanol interacts with NMDAR in the M domains with specific amino acids including Gly638 in the GluN1 subunit as well as Phe637 and Gly826 in the GluN2B subunit (2,3). Researchers are determining the location of the strongest NMDAR-ethanol interactions using amino acid substitutions. The Brown Deer High School SMART (Students Modeling A Research Topic) Team has designed a model of NMDAR using 3D printing technology to visualize the NMDAR-ethanol interactions. If researchers can develop molecules to help minimize the effect of ethanol on the brain, it could reduce the cost of alcoholism to society.

1. Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. (2015) *Am. J. Prev. Med.* 49: e73–e79.
2. Ren H, Zhao Y, Dwyer DS, Peoples RW. (2012) *J. Biol. Chem.* 287: 27302-27312.
3. Zhao Y, Ren H, Dwyer DS, Peoples RW. (2015) *Neuropharmacol.* 97: 240-250.