

THE MOLECULAR MYSTERIES OF ALCOHOL

It likely started with rotting fruit falling on the ground, as ancient humans observed unsuspecting birds and critters becoming intoxicated as they feasted on the fermenting juices.

“Alcohol is one of the oldest drugs — it’s been around since the dawn of time,” says Dr. Robert Peoples, an associate professor of biomedical sciences who is one of the leading experts on the molecular mechanisms through which alcohol produces its effects. “People have been drinking wine and beer for millennia, but it’s a hard drug to study because it acts at high concentrations.”

Yet what we still don’t know about this drug’s impact on the brain is of critical importance: Nearly 18 million Americans abuse or are dependent upon alcohol, and excessive alcohol use leads to more than 75,000 deaths each year, making it the third-leading preventable cause of death, according to the National Institute on Alcohol Abuse and Alcoholism.

Peoples has spent 20 years studying the molecular mysteries of alcohol use. A prolific researcher, he frequently publishes in journals such as *Proceedings of the National Academy of Sciences*, *The Journal of Biological Chemistry* and *Neuropharmacology*.

Peoples’ lab focuses on the NMDA receptor, which is a protein on the surface of nerve cells that allows ions such as sodium and calcium to enter the cells. The protein binds glutamate, one of the major neurotransmitters in the brain, and when it’s blocked by alcohol, it can cause problems with physical coordination, learning, memory and other brain functions.

“The question is: How does alcohol work on this protein in the brain?” Peoples says. “Where exactly is it binding, and how is it acting?”

Drugs act by binding to molecular targets. For neuroscientists, it helps if a drug binds tightly — but alcohol does not, which is why it’s difficult to study.

Only in the past couple of decades have researchers realized that alcohol affects nerve cells by binding to molecular targets on proteins instead of dissolving in cell membranes. Peoples’ research has revealed important insights into how alcohol interacts with the NMDA receptor. His lab has shown that alcohol affects NMDA receptors by inhibiting the opening and closing of the channel in the protein that allows ions to enter or exit the cell. Peoples has zeroed in on a handful of specific sites on the protein, and his ultimate goal is to identify new therapeutic targets.

“It’s going from the biophysics of this ion channel to how it will have an impact on human health,” he says. “It may be possible to design drugs that would be helpful in treating alcohol abuse.” — NSE

