New treatments may be on the horizon for individuals affected with drug addiction or depression. A.J. Robison, assistant professor in the Department of Physiology and the Neuroscience Program, is studying these often-related issues in his lab—with promising results.

A past project in the Robison lab focused on the role of a particular transcription factor, a protein known as ∆FosB, in the nucleus accumbens region of the brain (the “pleasure center”) and how it relates to the rewarding effects experienced by drug use. In more recent research, Robison’s lab is investigating how ∆FosB regulates gene expression in the hippocampus (the part of the brain important for learning) in response to cocaine, and how that affects the associations made between the drug and the environment in which it is used.

“One thing that makes cocaine an insidious drug—and this is true of heroin and other addictive drugs—is that users form indelible, strong associations between the drug and the context in which they use the drug,” Robison said.

The research team wants to determine how exposure to cocaine and the formation of those associations alter gene expression in the hippocampus.

Another study being carried out in the Robison lab involves depression and the mechanism of the action of antidepressants. In collaboration with the Viral Vector Core at MIT, Robison's team has developed a new technology to investigate just how ∆FosB works.

This new technology will enable researchers to determine which connections in the brain ∆FosB is modulating, and how those connections then regulate a specific depression phenotype or response to antidepressant treatment. It will help them understand which exact circuits underlie the problems with depression and devise means for manipulating those specific circuits, which could lead to more individualized and more targeted treatment plans.

“This is important because most of the current treatments for depression are systemic—drugs are taken orally or by injection—and they affect the whole body and the whole brain. Yet, fewer than 50 percent of patients have good responses to traditional antidepressant treatment,” Robison said.

The medical field is just beginning to develop more targeted treatments for depression, such as deep-brain stimulation, which involves placing electrodes into select regions of the brain.

“But this is very invasive, and it doesn’t work in all patients,” Robison said.

“If we can develop a real mechanistic understanding of how some of these kinds of depression occur, we may be able to develop a much more targeted means of treating certain aspects that are predominant in one person's depression versus another's. This could lead to much less invasive, and much more effective, means of treating the disease.”

Robison is careful to point out that his lab is not developing a “cure” for depression.

“We are trying to understand the etiology of the disease and the mechanism of the disease, as well as the mechanism of how current antidepressants work. Our goal is to advance and design those novel treatments in the long run.”

Mackenzie Thibault (left), a neuroscience senior, listens as A.J. Robison, assistant professor in the Department of Physiology and the Neuroscience Program, discusses brain circuitry involved in memory and reward with Andrew Eagle (far right), a postdoctoral fellow.