Genetic Tool to Treat Cocaine Addiction

T32 Training Grant faculty member Ming Xu and his colleagues have taken the first steps to developing cocaine-resistant mice. Using the CRISPR-based gene-editing platform to modify the DNA of skin cells, Dr. Xu and Xiaoyang Wu were able to create genetically modified mice that are less inclined to take cocaine than their counterparts, but are also immune to cocaine overdoses that killed mice without the same CRISPR-edited cells.

The process builds on previous work involving a modified enzyme called butyrylcholinesterase (BCHE), which is capable of naturally breaking down cocaine very rapidly. Unfortunately, its short half-life makes it ineffective in a clinical scenario, since it disappears before it has any long-term impact on the body’s response to cocaine. BCHE cannot be administered orally, which makes it ill-suited for use as a potential treatment. However, Wu and Xu found a way around this by demonstrating that modified skin cells can secrete BCHE into the bloodstream over a long period of time, and remarkably, these skin cells can be applied in the form of a skin graft.

Although this research is still early stages, it could provide a critical new tool to battle the effects of cocaine addiction in humans via a similar skin graft procedure.

Wu states “It will work, like in mice, by highly efficiently degrading cocaine as soon as it enters the blood circulation, so that little would reach the brain to produce consequences”. This might prevent initiation and continuation cocaine addiction, and maybe even reduce relapse in addicts.

A paper describing the work was recently published in the journal Nature Biomedical Engineering.