bodies to fentanyl and its analogs, for which they have applied for a provisional patent, Matyas says.

As the collaboration between WRAIR and NIDA got underway, Pravetoni, then at the University of Minnesota, and colleagues were in the early stages of their work on a vaccine for oxycodone, a main driver of opioid overdoses at the time. In response to shifting trends in overdose deaths over the past decade, the team is now developing a heroin vaccine and has received funding from NIDA to create vaccines and monoclonal antibodies against fentanyl and fentanyl analogs, the synthetic opioids largely driving the ongoing surge in overdose deaths. They hope to progress to clinical testing with one of these fentanyl candidates next year.

Meanwhile, in the current Phase 1a/1b trial of their oxycodone vaccine candidate funded by the HEAL Initiative, the

**VACCINE-INDUCED BLOCK**

Due to their small molecular size, opioids can cross the blood-brain barrier (BBB) to cause both the euphoria that makes such drugs so addictive and the adverse effects including the respiratory depression that can cause fatal overdose via inhibition of neural networks that regulate breathing (left panel). To fight opioid use disorder (OUD) and reduce overdose deaths, scientists have designed a handful of experimental vaccines, which are just beginning to enter human testing. These experimental vaccines involve a carrier protein studded with analogs of the opioid, called haptenes, combined with adjuvants that strengthen the overall immune response (middle panel). Antibodies generated against haptenes will bind to the opioid, blocking it from crossing the BBB due to the antibodies’ large size (right panel). The hope is that if people recovering from OUD receive a vaccine targeting their drug of abuse and then relapse, they will not experience respiratory depression that can lead to overdose or the euphoric effects that reinforce the drug-seeking behavior.