Pain management is one of the most important fields of research in modern medicine. Pain is not only a byproduct of most other ailments, it can significantly hamper the efficacy of treatments for those ailments because the patient’s tolerance for pain often needs to be addressed at the same time.

Alan Smrcka, the Louis C. Lasagna Professor in Experimental Therapeutics in the Department of Pharmacology and Physiology, is studying the way a particular class of proteins sends messages inside cells with the aim of allowing opiates to decrease pain more effectively, and with significantly fewer side effects.

“When opiates come in contact with a cell, a special receptor on the cell’s membrane gets activated,” says Smrcka. “That receptor releases a protein called a g-protein that acts like a key looking for doors in the cell it can unlock. Some of those doors lead to pain reduction, which is wonderful, but some lead to side effects we’d rather not have, like constipation or difficulty breathing. What I’m working on is a way to make that key fit only the doors we want, and none of the ones we don’t.”

Smrcka has found a number of molecules that can bind to select receptors inside the cell – the biochemical equivalent of jamming gum in the locks of certain doors so the g-protein key can’t fit. What makes the task so enormously difficult is that the “gum” must bind to only certain locks, and prevent only the right keys, otherwise the cell’s complex normal living functions can be compromised.

“It’s certainly tricky trying to find a way to keep one pathway open while blocking another,” says Smrcka. “But, if we can do it, and we’re seeing evidence that we can in the lab, then that means we should be able to get the same amount of pain reduction for a patient at a significantly lower dose of morphine or similar medication.”