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Opioids as analgesics are very effective in the control of severe pain. However, their addictive potential is so high that their overuse often leads to the development of drug dependence and sometimes to an overdose. Even with the proper use, opioids cause various side effects. The opioid mu receptor (MOR), which is the primary receptor for the analgesic effects of opioids, has been shown to contribute to the negative side effects of opioids. Unfortunately, few MOR antagonists are available for clinical use, and the efficacy of clinically used MOR antagonists has been controversial. Recently, we have found that a plant-derived triterpenoid, betulinic acid (BA), specifically binds to a MOR variant, MOR-3, with an affinity at least ten-fold higher than that for MOR and with little or no affinity for any other opioid receptor subtypes. This makes BA a very promising agent for the treatment of opioid dependence without causing any serious side effects. Indeed, we have shown in our initial studies that BA produces a very high antinociceptive potency (ED₅₀=0.1mg/kg) that is at least as potent as morphine (ED₅₀=0.2mg/kg). Thus, we propose to use a battery of behavioral tests to determine the efficacy of BA as an antagonist for MOR-3, a high-aff 2d92ce491b