**Development of opioid vaccines using bacteriophage virus-like particles**

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Oxycodone is the most abused prescription opioid and a common cause of opioid use disorder and overdose. Despite the availability of different treatment options, opioid overdose rates have skyrocketed to a staggering 80,000 deaths in 2021. Vaccines against opioids have been proposed as a novel strategy for preventing overdose and several studies have established the feasibility of this approach. Here, we report our efforts to engineer a vaccine against oxycodone that elicits high-titer antibodies with protective functionality against oxycodone. We accomplish this using a bacteriophage Qβ virus-like particle (VLP) platform to display oxycodone in a highly immunogenic and multivalent format. The repetitive nature, small particulate size, and excellent safety profile of Qβ VLPs makes them a promising platform for vaccine design. The oxycodone hapten was chemically modified to include a short peptide linker (GGGG-C) to enable conjugation to Qβ VLPs. Mice and rhesus macaques were immunized with Qβ-oxycodone or unconjugated Qβ control. Qβ-oxycodone elicited high-titer antibodies after one immunization, with high-avidity IgG antibodies elicited after two immunizations. In future studies, we will investigate drug distribution in the blood and brain, as well as protection from oxycodone-induced anti-nociception and opioid induced respiratory depression.