A bacteriophage virus-like particle vaccine against heroin generates protective antibody responses

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Opioid use disorder (OUD) and opioid overdose are urgent public health crises, with opioid overdose rates tripling within the last decade in the United States. Current treatments have limited efficacy, and challenges associated with implementation. Vaccines against opioids have recently been proposed as novel treatments, with some vaccine strategies showing promising pre-clinical data. Here, we report our efforts to engineer a vaccine against heroin that elicits high-titer and long-lasting antibodies with protective functionality. We utilized bacteriophage Qβ virus-like particles (VLPs) to display drug targets in a highly immunogenic and multivalent format. The active metabolites of heroin, morphine and 6-aceyl-morphine, were chemically modified to include a short peptide linker (GGGG-C) allowing for chemical conjugation to Qβ VLPs. BALB/c mice (n=6) were then immunized with 2 doses of Qβ-morphine (20μg), Qβ-6-acetyl-morphine (20μg), or a combination vaccine (20μg Qβ-morphine + 20μg Qβ 6-acetyl-morphine) . We studied kinetics of elicited antibody responses via Enzyme Linked Immunosorbent Assays (ELISAs) and show the generation of high-titer antibodies against morphine and 6-acetyl-morphine. A dose response study was conducted in naïve animals to determine the heroin dose used in subsequent anti-nociception challenges. Animals were challenged with subcutaneous heroin (0.5mg/kg, as determined via the dose response study) and anti-nociceptive responses were studied in tail-flick assays. We found that both the Qβ-6-acetyl-morphine and the combination vaccine candidates significantly reduced the anti-nociceptive effects of heroin in a tail flick assay.