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The Use of Single-Chain Variable Fragments (scFv) to Reverse Cardiopulmonary and Antinociceptive Effects of Fentanyl in Male Mice

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Abstract Text: Opioid use disorder and opioid-related overdose deaths continue to serve as a worldwide health concern and were further exacerbated by the COVID-19 pandemic. Current FDA-approved treatments for opioid overdose are limited to opioid receptor antagonists and may produce untoward effects. Immunotherapeutics such as monoclonal antibodies (mAb) have been proposed as additional treatment for opioid overdoses. The current study investigated the potential of anti-fentanyl single-chain variable fragments (scFv) to reverse the cardiopulmonary and antinociceptive effects of fentanyl. Male BALB/c mice (n = 5 per group) were administered subcutaneous fentanyl (0.1 mg/kg) and 15 minutes later were administered either subcutaneous saline (10 ml/kg), subcutaneous naloxone (0.1 mg/kg) or scFv (40 mg/kg) delivered intramuscularly, intravenously, or subcutaneously. Heart rate, breath rate, and oxygen saturation were quantified in 5-minute intervals, and thermal nociception in 15-minute intervals, for a total of 60 minutes. Fentanyl significantly reduced heart rate, breath rate, oxygen saturation, and thermal nociception. Intramuscular and intravenous injections of scFv rapidly reversed the cardiopulmonary and antinociceptive effects of fentanyl, returning them back to baseline. Similarly, subcutaneous administration of scFv produced a less rapid, but complete, reversal of the effects of fentanyl. Administration of scFv was able to fully reverse the cardiopulmonary and antinociceptive effects of fentanyl. Future studies will determine whether scFvs produce an opioid withdrawal syndrome akin to that produced by naloxone, as well as the selectivity of this scFv to bind fentanyl relative to other structurally similar fentanyl analogs with the ultimate goal being the development of clinically effective immunotherapeutic treatments for individuals suffering from opioid use disorders.