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**Assessing the impact of opioid exposure on lung immune function and in acute ICU care after drug overdose**

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The opioid use disorder (OUD) epidemic is one of the largest problems facing public health. Patients who survive overdose are often cared for in the Intensive Care Unit (ICU) environment with respiratory and other organ failure, and often develop infections including pneumonia. Through single cell studies, we can now identify which cells in the lung immune system express receptors for opiates, and explore the impact of such drugs on the epigenetic reprogramming and immune function in these cells. Preliminary data indicates that alveolar macrophages are the only lung cells which express opiate receptors. Opioids modulate levels of the cellular second messenger cyclic AMP (cAMP). Macrophages require metabolic and genetic reprogramming to respond to infection, which is deranged by cAMP modulation, conferring potential risk in OUD patients. This finding may provide mechanism for prior studies showing opioid impairment of macrophage defensive effector function. Clinically, patients in the ICU after opioid overdose have a significantly higher burden of critical illness non-opioid overdose cases with higher circulating levels of high risk cytokines like IL-6. These studies may help us better understand the impact of OUD on immunity and inform our perspective on drug overdose in the acute care setting. We hope to reveal novel pathophysiology and risk variants for these patients and enable the implementation of personalized medicine strategies to address this urgent public health problem.