The Histone Methyltransferase SETDB2 Regulates Inflammation in Normal and Diabetic Wound Repair

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ABSTRACT IMPACT: Our data reveal a histone modifying enzyme involved in regulating inflammation that may be a novel target for treating non-healing diabetic wounds. OBJECTIVES/GOALS: We investigate molecular mechanisms that regulate the inflammatory phenotype of macrophages in normal and diabetic wound healing. Our goal is to identify novel pathways that may be used to better treat diabetic patients with non-healing wounds. METHODS/STUDY POPULATION: We utilize normal and transgenic murine models on standard chow or high-diet to identify chromatin modifying enzymes involved in regulating macrophage function during wound healing. We validate our murine studies with human blood monocytes or wound macrophages from diabetic patients undergoing limb amputation surgery. RESULTS/ANTICIPATED RESULTS: We have identified the histone methyltransferase SETDB2 as a regulator of inflammation in normal and diabetic wound macrophages. We found that SETDB2 was dependent on IFNβ signaling and that both IFNβ and Setdb2 expression were impaired in diabetic wound macrophages. Further, we show that SETDB2 regulates inflammatory response and immune cell trafficking pathways. We also show that SETDB2 genomic localization is dependent on **NFκΒ** deposition of the promoter. DISCUSSION/SIGNIFICANCE OF FINDINGS: Our results indicate that SETDB2 is a regulator of macrophage plasticity and that SETDB2 expression is impaired in diabetic wound macrophages leading to hyper-inflammatory response and delayed wound healing. These data provide a novel potential therapeutic pathway for treating non-healing diabetic wounds.

Brain Mapping Addiction

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ABSTRACT IMPACT: Gaining a better understanding on the role of opioids in opioid use disorder (OUD) can help us find better diagnostics, treatments, and procedures to treat the disorder. OBJECTIVES/GOALS: While we are familiar with brain areas and pathways that are implicated in opioid use disorder (OUD), we do not have a full understanding of the neural circuits activated upon drug exposure. METHODS/STUDY POPULATION: In order to identify areas of the brain most activated by opioids, we ran a pilot study using transgenic cFos-GFP mice that were injected with saline or heroin and examined the brain-wide activity patterns using a quantitative high-resolution mapping method. We observed many brain regions highly activated upon drug exposure. To examine cFos based brain activation in rats,