potential in the realm of infectious diseases. OBJECTIVES/GOALS: The role of IFNLR1 receptor dynamics and plasticity in regulating the type-III IFN response is largely unknown. As a specific, powerful component of innate immunity, understanding how the type-III IFN system is regulated could lead to the development of novel therapeutic targets and strategies to face a multitude of viral illnesses. METHODS/STUDY POPULATION: To facilitate our investigation, we will generate doxycycline-inducible FLAG-tagged IFNLR1-expression plasmids representing all known transcriptional variants. These plasmids will allow us to: 1) Evaluate the effect of IFNLR1 surface abundance on the type-III IFN transcriptional profile and 2) Assess the extent of IFNLR1-FLAG co-localization with several notable intracellular structures using immunofluorescence, before and after stimulation with IFNL3. RESULTS/ANTICIPATED RESULTS: We have successfully generated three IFNLR1-FLAG transcriptional variants and confirmed inducible-expression and function in vitro. We are currently assessing the role of surface abundance, internalization, differential isoform expression, and trafficking. DISCUSSION/SIGNIFICANCE OF FINDINGS: By completing this study, we hope to provide a more nuanced understanding of the type-III IFN system, thereby exploring its therapeutic potential in the realm of infectious diseases.

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 inflammation in normal and diabetic wound macrophages. We found that SETDB2 was dependent on IFNβ singaling 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.

The Signaling Axis of Tumor Suppressor LKB1 in Triple Negative Breast Cancer*

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ABSTRACT IMPACT: Identifying an important pathway in treatment resistant TNBC will allow for the future development of clinical therapeutics specific for this disease. OBJECTIVES/GOALS: Triple Negative Breast Cancer (TNBC) is a subtype of breast cancer characterized by negative expression of estrogen receptor, progesterone receptor, and HER2/neu amplification. It resists therapies and has a high recurrence rate after resection. The goal of my research is to identify & characterize a TNBC pathway for future development of therapies. METHODS/STUDY POPULATION: The project uses a combination of cell lines, patient derived xenograft (PDX) models, as well as patient databases. Standard cellular and molecular biology techniques will be used including: Cell culture, qPCR, western blotting, and flow cytometry. RESULTS/ANTICIPATED RESULTS: LKB1 is a master kinase that activates 14 possible downstream kinases. The signaling pathway has been demonstrated to play a role in energy homeostasis and metabolism. Mutation of LKB1 signaling results in Peutz-Jeghers Syndrome and is associated with neoplasias of the lung, pancreas, and breast. Based on preliminary analysis, overexpression of LKB1 by shRNA in TNBC cell lines results in suppression of EMT and reduction of the cancer stem cell population. Additional studies show that LKB1 overexpression has no effect on growth rate in 2D culture while significant reduction in 3D mammosphere formations can be seen. Downstream studies using commercially available SIK1 inhibitor HG-9-91-01 is able to induce a larger fraction of CSC from reduced LKB1 overexpression as well as from baseline levels. DISCUSSION/SIGNIFICANCE OF FINDINGS: Overall, our results suggest that LKB1 acts through SIK1 to suppress EMT and the generation of cancer stem cells. This results in reduced cancer functionality, as evidenced by inhibition of mammosphere formation. These results establishes a foundation for future mechanistic studies on the LKB1 axis and its mechanisms in TNBC.

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,