bacteria growth over time to see how the donor microbiome would change during a 24 hour experiment in anaerobic conditions. Finally, we anticipate seeing increases in dATP with a Prevotella or Dialister supplemented donor microbiome compared to baseline donor microbiome. DISCUSSION/SIGNIFICANCE: The addition of vaginal dysbiosis to tissue model will increase accuracy of prediction of 100% protective TFVdp concentrations and is likely to provide a translational model that can be used to improve TFV-based PrEP in women and streamline development of future PrEP candidates, bringing more prevention options to women and ending the HIV epidemic.

300

Impact of the type of mechanical circulatory support (MCS) prior to transplant on development of post-orthotopic heart transplantation (OHT) infections

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OBJECTIVES/GOALS: In 2018, the United Network for Organ Sharing began prioritizing patients on temporary MCS over those on durable MCS for OHT in an effort to prioritize sicker patients and decrease waitlist mortality. We explored the impact of this change by examining if the type of MCS prior to transplant affects the risk of post-transplant infection. METHODS/STUDY POPULATION: We will conduct a retrospective cohort study of approximately 350 patients that have undergone OHT at Tufts Medical Center between January 2014 and July 2021 who survived at least 72 hours post-transplant and have minimum post-transplant follow-up of one year or time to death if before one year. Chart review will determine the type of MCS in place prior to transplant and the occurrence of infections within one year of transplant. Data will also be collected on patient's age, sex, medical comorbidities, lab values, and open chest management practices. We will examine differences in the incidence rates of a composite outcome (blood stream infection, invasive fungal infection, skin and soft tissue infection of device sites, and mediastinitis) between patients that were on temporary versus durable MCS. RESULTS/ANTICIPATED RESULTS: We anticipate that this study will show a greater frequency of infections of all types in patients that received temporary as compared with durable mechanical circulatory support prior to transplantation. We will use Cox proportional hazards survival models to model multivariable relationships for predictors of infection. DISCUSSION/SIGNIFICANCE: This study will provide insights into the magnitude and type of infectious complications that patients experience after OHT and the impact that type of MCS and other factors have on their outcomes. The data obtained may have implications for choice of mechanical device prior to undergoing OHT surgery as well as antimicrobial prophylaxis.

301

Inhibition of lysine-specific histone demethylase 1A (KDM1A/LSD1) attenuates DNA double strand break repair and enhances efficacy of temozolomide in glioblastoma

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OBJECTIVES/GOALS: Glioblastoma (GBM) patients face a poor prognosis. Glioma stem cells (GSCs), a chemo resistant GBM subpopulation, possess enhanced DNA repair and elevated levels of epigenetic modifier KDM1A. This study aims to establish the significance of KDM1A in DNA repair and determine the potential of novel KDM1A inhibitor NCD38 to enhance TMZ efficacy in GSCs. METHODS/STUDY POPULATION: Patient derived GSCs were obtained via IRB-approved protocol from patient samples at UT Health San Antonio. KDM1A knockdown and knockout cells were generated by transduction of validated KDM1A-specific shRNA or gRNA, respectively. Brain bioavailability of KDM1A inhibitor NCD38 was established using LS-MS/MS. Effect of combination of KDM1A knockdown, knockout, or inhibition with TMZ was studied using cell viability, neurosphere, and self-renewal assays. Mechanistic studies were conducted using CUT&Tag-seq, RNA-seq, immunofluorescence, comet, Western blotting, RT-qPCR, homologous recombination (HR) or non-homologous end-joining (NHEJ) DNA repair reporter assays. In vivo efficacy of KDM1A knockdown or inhibitor alongside TMZ treatment was determined using orthotopic murine GBM models. RESULTS/ANTICIPATED RESULTS: KDM1A knockdown, knockout, or inhibition increased efficacy of TMZ in reducing cell viability and self-renewal of GSCs. Pharmacokinetic studies demonstrated KDM1A inhibitor NCD38 is readily brain penetrable. CUT&Tag-seq studies revealed KDM1A is enriched at DNA repair gene promoters. RNA-seq studies suggest KDM1A inhibition reduces DNA double strand break repair gene expression, with these findings validated using RT-qPCR and Western blotting. Knockdown, knockout, or inhibition of KDM1A attenuated HR and NHEJ-mediated DNA repair capacity. Immunofluorescence and comet assay support findings of increased DNA damage in NCD38/TMZ combination treated GSCs. Importantly, KDM1A knockdown or inhibition enhanced efficacy of TMZ and significantly improved survival of orthotopic GBM tumor-bearing mice. DISCUSSION/SIGNIFICANCE: Our results show compelling evidence that KDM1A is essential for DNA repair in GSCs and that KDM1A inhibition sensitizes GBM to TMZ via attenuation of DNA repair pathways. These findings suggest combination of KDM1A inhibitor NCD38 with TMZ could serve as a promising novel therapeutic strategy that can be translated to improve GBM patient outcomes.

303

Investigation of the antibacterial and regenerative properties of a novel AHA dental coating for the treatment of deep caries*

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OBJECTIVES/GOALS: Our objective is to investigate the antibacterial and regenerative properties of a novel AHA dental coating for the prevention and treatment of deep caries (cavities). Further, we aim to investigate and compare these properties through in vivo

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