

tests. Identifying specific proteins with the potential to become a preventive test should eventually lead to a reduction in morbidity and mortality of PC. The results of this work should lay the foundation that can guide future research.

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### Identifying Gaps in Elderly Fecal Incontinence Management

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**OBJECTIVES/GOALS:** Fecal incontinence is associated with increased caregiver strain, reduced patient dignity and diminished quality of life. A spectrum of incontinence exists, along with a paucity of available solutions for patients and their caregivers. This research aims to stratify this space and identify gaps within the existing solution landscape. **METHODS/STUDY POPULATION:** To understand this problem, a literature review was performed with key search terms specific to fecal incontinence. These included, anal incontinence epidemiology, fecal incontinence in nursing homes, and incontinence management. To determine gaps within the existing solution landscape, key search terms related to existing solutions for fecal incontinence were also included. These included, fecal management systems, rectal incontinence therapies, and anorectal incontinence procedures. To perform a population segmentation, white papers, review articles, and cross-sectional studies were reviewed to break down the burden of incontinence in older adults living in nursing facilities and in the community. **RESULTS/ANTICIPATED RESULTS:** Two unaddressed populations were identified, the first being independent adults over the age of forty, particularly women, who suffer from frequent, bothersome incontinence. These 1.2 million patients are active, living at home, and they restrict their daily activities due to incontinence. However, there are several durable and effective solutions for patients who have sufficient sphincter tone or who are surgical candidates. The second population identified are caregiver dependent older adults residing in nursing facilities who suffer from severe incontinence. This population of 160,000 is affected more severely by consequences of fecal and are poorly served by solutions that are largely absorptive such as diapers and pads. **DISCUSSION/SIGNIFICANCE:** Although two populations were identified, caregiver dependent older adults residing in nursing homes were identified to have a significant unmet need within incontinence care. Current solutions are onerous and transient, preventing ease and duration for use by caregivers and nurses.

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### Identifying Opportunities and Challenges for Translational Informatics Approaches to Real-World Data: A Diabetes Case Study

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**OBJECTIVES/GOALS:** Diabetes is a group of chronic metabolic diseases and significant gaps remain in our understanding of disease etiology, treatment regimens, and diabetes-related complications. The objective of study is to demonstrate how informatics techniques can leverage real-world data for diabetes research and identify barriers for implementation. **METHODS/STUDY POPULATION:** We evaluated informatics applications of real-world data in diabetes research conducted by the Facelli Research Group. The types of real-world data

were categorized into clinical records, diabetes-related repositories, wearable sensors, and other data sources. Translational informatics applications were characterized into thematic groups of 1.) use of electronic health records, registries, and claims and other data sources to generate real-world evidence, 2.) evolution of novel methods to accelerate generation and use of real-world data, and 3.) infrastructure to support the generation and use of real-world data in translational science. A literature review is being conducted to identify additional articles meeting these themes focused on diabetes research. **RESULTS/ANTICIPATED RESULTS:** 6 research projects were included for analysis. The diabetes-focus spanned type 1 diabetes, type 2 diabetes, and general diabetes mellitus. Informatics methods included machine learning and data mining while real-world data sources included electronic medical records, the Environmental Determinants of Diabetes in the Young (TEDDY) study, continuous glucose monitors, and the U.S. Environmental Protection Agency (EPA) air pollution monitors. Overall, computability of real-world data, linkage of medical concepts to standardized terminologies, volume of data, and adoption of novel artificial intelligence methods were major determinants of successful implementation. Future work will systematically evaluate informatics applications of real-world data in diabetes from the academic community at large. **DISCUSSION/SIGNIFICANCE:** Translational informatics approaches are poised to leverage real-world data and better understand diabetes etiology, treatment regimens, and diabetes-related complications. By understanding barriers and opportunities for informatics methods, we can expedite translational applications in diabetes research.

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### Identifying vaginal microbiome profiles that influence tenofovir distribution in the female genital tract\*

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**OBJECTIVES/GOALS:** An ex-vivo tissue model has been developed to predict target concentrations of tenofovir diphosphate (TFVdp; active metabolite of tenofovir) but has not been utilized to see how vaginal dysbiosis affects TFVdp/dATP exposure in female genital tract (FGT). My central hypothesis is that presence of specific anaerobic bacteria will increase dATP in FGT. **METHODS/STUDY POPULATION:** De-identified HIV-negative cervical tissues from women undergoing gynecological surgeries will be procured and a punch biopsy will be used to create explants. TFVdp/dATP concentrations were both tested in both aerobic and anaerobic conditions after a 24-hour incubation in tenofovir (TFV) to determine any changes between conditions. TFVdp/dATP in cervical tissue was be measured using LC-MS. Next, media and explants were collected at baseline to characterize donor microbiome for 6 donors. 16S microbiome sequencing was performed on extracted DNA to obtain the relative abundances of each bacteria species present. To test changes in dATP/TFVdp due to the microbiome, explants will be incubated in TFV for 24 hours with Prevotella and Dialister to specifically see how microbiomes dominated by these taxa affect dATP. **RESULTS/ANTICIPATED RESULTS:** There was no significant difference in TFVdp formation between aerobic and anaerobic conditions after a 24-hour tenofovir incubation ( $p = 0.2$ ) for 8 donors. dATP was not quantifiable at 24 hours in explants, so explants are being collected before 24hrs during a TFV incubation to determine how quickly dATP depletes after collection. We were able to characterize the donor microbiome in media and tissue at baseline and 24hrs which had inter variability. We did not see any presence of Prevotella or Dialister in any donors. We are working on characterizing

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.

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### **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.

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### **Inhibition of lysine-specific histone demethylase 1A (KDM1A/LSM1) 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.

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### **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