frozen. Frozen aliquots will be shipped to the Metabolite Profiling Facility at Purdue University and the Mayo Clinic Department of Laboratory Medicine and Pathology for SCFA and bile acid measurements, respectively. Analysis of fecal microbiota will be performed in the research laboratory of Dr David Nelson in collaboration with bioinformatics expertise affiliated with the Nelson lab. Colonic transit time will be measured with the previously validated method using radio-opaque markers. Generalized linear models will be used as the analysis framework for comparing study endpoints among groups. RESULTS/ANTICIPATED RESULTS: This study seeks to examine the innovative concept that specific microbial signatures are associated with increased fecal excretion of organic acids to provide unique insights on a potential mechanistic link between altered intraluminal organic acids and fecal microbiota. DISCUSSION/SIGNIFICANCE OF IMPACT: Results may lead to development of targets for novel therapies and diagnostic biomarkers for IBS, emphasizing the role of the fecal metabolome.

2006

Formative evaluation and adaptation of a safe sleep intervention for infants in rural underserved communities

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OBJECTIVES/SPECIFIC AIMS: This abstract describes a recently-funded 2 year study that aims to: (1) explore the community advisors' perspectives of the safe sleep intervention's acceptability, feasibility, and adaptability using focus groups and key informant interviews. (2) Adapt the selected safe sleep interventions (SSI) and identify promising implementation strategies to support it through an evidence-based quality improvement process with a multistakeholder group. METHODS/STUDY POPULATION: Background sudden unexpected infant death (SUID) is the leading cause of post-neonatal infant death in the United States. Sudden infant death syndrome (SIDS), accidental suffocation and strangulation in bed account for over 50% of SUID, leading to recommendations for supine sleep position and safer sleep environments for infants. However, despite significant reductions in SIDS after "back to sleep" and "safe to sleep" campaigns, significant racial and urban-rural disparities persist. In 2015, the rural-urban crude death rate ratio was 4:1 and Black infants are twice as likely to die from SUID as White infants. Adherence to safe sleep recommendations is highly variable and a number of hospital and community-based interventions have been suggested to improve knowledge and change parent behavior. Hospital programs to promote safe sleep education and policies may serve to educate families about safe sleep, but may not be uniformly available in rural and underserved areas. The AAP evidence-based safe sleep guidelines have demonstrated reductions in SIDS and SUID when child caregivers adhere to them. Community-based SSI, including safety baby showers, promote safe sleep practices, but barriers may exist for participation, especially in rural areas. Partnering with community groups serving a high risk area, we will explore the barriers and facilitators to more widespread safety baby shower (SBS) delivery/adoption in rural underserved communities (RUC). Observation of the evidence-based SBS as it is currently delivered, focus groups and key informant interviews will be conducted with program leaders and participants. Based on this knowledge and using an evidence-based development process, we will adapt the SBS and identify implementation strategies to support its uptake in RUC. RESULTS/ANTICIPATED RESULTS: We expect to develop a modified safe sleep intervention that reaches more expectant and new mothers is more efficient at delivering safe sleep guidelines to rural community members and can be more readily adopted and implemented by RUC. Supporting implementation strategies will be identified during the formative evaluation. DISCUSSION/SIGNIFICANCE OF IMPACT: Developing a safe sleep intervention adapted for the local context through a collective decision-making process between intervention experts and local community advisors will potentially improve safe sleep guideline delivery and adherence in RUC. The next study will pilot test the effectiveness of the adapted safe sleep intervention with identified supporting implementation strategies.

2066

Functional characterization of mutant BRCA1

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OBJECTIVES/SPECIFIC AIMS: The objective of this work is to determine the mechanistic consequences of BRCA1 mutants in inter-strand crosslink (ICL) repair. METHODS/STUDY POPULATION: Our lab uses Xenopus egg extracts to study ICL repair. These extracts can be depleted of endogenous BRCA1 by immunoprecipitation. The goal of this work is to rescue endogenous depletion with in vitro translated, wild type BRCA1. Once achieved, we can supplement the depleted extract with BRCA1 mutants to access their function in ICL repair. RESULTS/ANTICIPATED RESULTS: We hypothesize that the BRCT and RING domain mutations will abrogate ICL repair, while mutations in the coiled coil region will not affect repair. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings will have an immense impact on the understanding of BRCA1 domains. Importantly these results will spur personalized therapy of BRCA1 mutants by showing which domains are sensitive to cross-linking agents.

2408

Genital microbiomes of women with recurrent bacterial vaginosis and their regular male sexual partner

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OBJECTIVES/SPECIFIC AIMS: Epidemiologic data suggest that BV is sexually transmitted with male partners colonized or infected with the responsible organism(s). The objective of this study was to compare the genital microbiota of women with recurrent BV and their regular male sexual partner using 16S rRNA gene sequencing and quantitative PCR targeting BV-candidate bacteria (*Gardnerella vaginalis*, *Atopobium vaginae*, BVAB1-3, Sneathia, Leptotrichia, and Megasphaera type 1). METHODS/STUDY POPULATION: Women with recurrent BV ($\geq$3 prior episodes, including a current episode) and their regular male partner participating in a BV treatment trial and providing genital specimens (women: vaginal; men: urethral, coronal sulcus, urine) at enrollment were included. Male specimens for each participant were pooled. 250 bp 16S rRNA V4 region PCR amplicons were sequenced and analyzed using the QIIME pipeline. Taxonomy was assigned using the RDP Classifier against a modified Greengenes database with additional vaginal taxonomies added. An average relative abundance cutoff of 0.5% was used for analysis. qPCR was also performed for specific BV-candidate bacteria. Spearman correlation coefficients were used to investigate associations between all genital bacteria in addition to BV-candidate bacteria between partnerships. To determine positive associations between partnerships, the Wilcoxon signed-rank test was used. RESULTS/ANTICIPATED RESULTS: In total, 45 partnerships were included. Mean partnership age was 31.3 (SD = 7.9), 91.1% partnerships were African-American. The majority of partnerships (70.0%) reported condomless sex during the past 3 months. Regarding 16S data, 37 genital bacteria had an average relative abundance of $\geq$0.5%. The average Spearman correlation across all 45 partnerships was 0.28 (SD = 0.27) (median = 0.27, minimum = $-$0.21, maximum = 0.84). Overall, a positive association of all genital bacteria existed across the partnerships ($p < 0.0001$). However, regarding specific BV-candidate bacteria, Spearman correlation tests for *G. vaginalis*, *A. vaginae*, *Prevotella bivia*, Megasphaera type 1, BVAB1, and BVAB2 were nonsignificant. In contrast, *Sneathia* spp. were positively correlated between partnerships ($r = 0.37$, $p = 0.01$). With regards to qPCR results, RNA Cq analyses provided significant evidence for a linear association between male and females for only *A. vaginae* ($r = 0.52$, $p = 0.006$). DISCUSSION/SIGNIFICANCE OF IMPACT: In monogamous heterosexual couples in which the female has BV, the vaginal microbiota of women and the penile/urine microbiota of men were significantly correlated, particularly with regards to *Sneathia* spp. and *A. vaginae*, supporting the hypothesis that BV-associated bacteria are exchanged during sex.

2543

High concentrations of CXCL12 decrease pancreatic adenocarcinoma growth

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OBJECTIVES/SPECIFIC AIMS: We hypothesized that CXCL12, as a biased dimer variant or secreted at dimer-dominant concentrations, would influence PDAC growth and progression. METHODS/STUDY POPULATION: PDAC cells were genetically manipulated to express dimer-promoting levels of CXCL12. These cells were studied in vitro or orthotopically implanted into the

https://doi.org/10.1017/cts.2018.79 Published online by Cambridge University Press

mouse pancreas for in vivo studies. As a second approach, recombinant wild-type or engineered CXCL12 monomer or dimer proteins were applied to cells in culture or administered intra-peritoneal to study the effects on tumor growth. RESULTS/ANTICIPATED RESULTS: Mice engrafted with CXCL12-expressing cells had a better survival rate, delayed tumor growth and smaller tumors. Tumors from these mice had significantly less proliferation, measured by Ki-67 staining. In vitro analysis of CXCL12-expressing cells showed decreased viability and growth rates. Percent of cells in the cell cycle G2 phase was also decreased, suggesting cell cycle progression blockade. Viability of human PDAC cells dose-dependently declined upon wild-type CXCL12 treatment, with the non-motile dimer-dominant dose (1000 nM) exhibiting maximal effect. Treatment in an allogeneic mouse model of PDAC with locked-dimer CXCL12, but not wild-type, reduced tumor burden. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results support the notion that biased CXCL12 signaling may be therapeutically exploited to limit pancreatic cancer progression.

2070

High-intensity focused ultrasound (HIFU) can be used synergistically with tamoxifen to overcome resistance in preclinical and patient derived xenograft models

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OBJECTIVES/SPECIFIC AIMS: The goal of this study is to evaluate a potential strategy to overcome tamoxifen (tam) resistance by using tam in combination with high-intensity focused ultrasound (HIFU). Tam is the most commonly used anti-cancer therapeutic agent in estrogen receptor positive (ER+) breast cancer (BC) which accounts for ~70% of BC cases. Tam treatment decreases a woman's risk of recurrence by 50%; however, BC that is initially responsive to tam often develops resistance. METHODS/STUDY POPULATION: HIFU deposits acoustic energy locally to a cancerous region, which induces strong vibrations of molecules inside and outside of the cells. The resulting absorption causes rapid heating and mechanical disruption. This clinically relevant, noninvasive, and nonionizing physical force modality, has been shown to synergistically enhance chemical anticancer therapies. RESULTS/ANTICIPATED RESULTS: In this study we found that treatment of MCF7 cells with HIFU and tam has additive antiproliferative effects and mediates increased cell death. Additionally, we used tam resistant (TR) MCF7 cells that had been exposed to low-dose tam over time until they acquired resistance. When MCF7 TR are treated with tam there is no change in viability; however, treatment with HIFU in combination with tam decreased viability of both MCF7 and MCF7 TR to 19% and the viability of the cell lines was indistinguishable. We next evaluated the effect on MCF7 Y537S mutant ESR1, where ER is mutated to be constitutively active. Treatment of MCF7 Y537S had no significant decrease in viability of combination therapy compared with viability after HIFU alone. Analysis of ERalpha gene expression showed that HIFU treatment increased ERalpha expression in MCF7 TR cells, thus resensitizing these cells to tam and allowing these therapies to work synergistically. Our team developed a system to evaluate the potential of this combination of therapies in a patient-derived xenografts (PDX) model. PDX have emerged as a novel translational tool for cancer research with the potential to more accurately recapitulate the molecular and behavioral aspects of cancer. The WHIM20 PDX is a tamoxifen resistant tumor where the patient developed the Y537S mutation in ESR1. Ex vivo experiments on PDX tumor pieces demonstrated that combination therapy of HIFU and tam work synergistically to increase cell death of these tumors. Further, cryogenic-scanning electron microscopy was utilized to directly demonstrate the physical disruption to both cellular and tumor microenvironment post exposure to combination treatment. DISCUSSION/SIGNIFICANCE OF IMPACT: These studies present a novel translational strategy to overcome tamoxifen resistance in ER+ BC.

2459

Hippocampal network disruption in early amyloid pathology

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OBJECTIVES/SPECIFIC AIMS: We aim to show that amyloid accumulation in an animal model of Alzheimer's disease leads to a preferential disruption of inhibitory parvalbumin-expressing interneurons, and the peri-neuronal nets that surround them, resulting in downstream network alterations to potentially explain early mechanisms of memory impairment in the disease. METHODS/STUDY POPULATION: We employ the 5xFAD mouse model of familial Alzheimer's disease crossed with transgenic mouse lines which fluoresce red or green in specific neuronal populations. We conducted immunostaining and immunoblotting in amyloid accumulating animals compared with healthy littermate control. Future experiments will be performed in human post-mortem tissue to translate these results from mouse model to the human population. Electrophysiological recordings from acute mouse brain slices were conducted as a functional assay. RESULTS/ANTICIPATED RESULTS: Preliminary results indicate that PNNs are disrupted and that activity-associated levels of PV are reduced. Both inhibitory PV and excitatory pyramidal cell populations exhibit altered spiking and synaptic activity during sharp wave ripple events. DISCUSSION/SIGNIFICANCE OF IMPACT: By elucidating the specific neuronal sub-type that is responsible for hippocampal network disruption, future studies could attempt a targeted optogenetic or pharmacological intervention to restore network activity important for memory consolidation.

2338

Identifying the genetic determinants of human brown adipose tissue

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OBJECTIVES/SPECIFIC AIMS: Brown adipose tissue (BAT) increases energy expenditure by dissipating chemical energy as heat. The combustion of glucose and lipids produces beneficial metabolic effects and renders BAT an attractive target to battle obesity and associated diseases. The majority of adults do not display active BAT on positron emission tomography (PET) without prior cold exposure. Interestingly, a fraction of individuals with BAT positive PET scans exhibits excessive BAT (eBAT) activity, indicating a possible underlying genetic contributor. We aim to identify genetic determinants of BAT activity by studying individuals with eBAT activity using next-generation sequencing. A cellular model will be used to validate variants and perform in-depth pathway analysis. METHODS/STUDY POPULATION: We performed a retrospective review of PET scans over a period of 12 months in patients presenting with suspected or diagnosed cancer (n = 20,348). The distribution of BAT positive individuals (n = 1251) was used to implement a threshold to define eBAT activity. Samples from prospectively recruited individuals with BAT activity above the threshold will undergo whole exome sequencing. Variants associated with eBAT activity will be engineered into an immortalized BAT cell line using CRISPR to validate results and perform in-depth pathway analysis. RESULTS/ANTICIPATED RESULTS: We expect to identify genetic variants associated with eBAT. Studying the effects of these variants on thermogenesis followed by in-depth pathway analysis in genetically engineered cellular and mouse models may enable us to find new regulators of BAT activity. These findings may eventually contribute to the development of new drugs targeting obesity and its sequelae. DISCUSSION/SIGNIFICANCE OF IMPACT: The contribution of genetic factors to individual BAT activity is currently unknown. Identifying individuals with eBAT on PET scans and studying the underlying genetic determinants may provide the foundation for the discovery of new pathways for BAT activation.

2050

Identifying the role and immunobiological mechanisms of Fli-1 mediated pathogenicity in graft Versus host disease

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OBJECTIVES/SPECIFIC AIMS: Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a curative procedure for hematological malignancies. Chronic graft Versus host disease (cGVHD) is a lethal complication that often develops after allo-HCT. Fli-1 is an aberrantly expressed protein in cancers including erythroleukemia and melanoma, while being implicated in pathogenesis of systemic lupus in mice and humans, a disease with marked similarity to cGVHD. METHODS/STUDY POPULATION: cGVHD was induced using hematopoietic cells from conditional knock-out mice deficient for the fli-1 gene specifically on T cells and progression of cGVHD in murine allo-HCT recipients was

https://doi.org/10.1017/cts.2018.79 Published online by Cambridge University Press