

normal parenchyma they remodel the composition and ultrastructure of the surrounding extracellular matrix (ECM), suggesting that the native (i.e., "normal") microenvironment is not ideal for their survival and proliferation. Recent reports describe suppressive and/or lethal effects of mammalian ECM hydrogels derived from normal (nonneoplastic) sources upon various cancer types. ECM-based bioscaffolds placed at sites of neoplastic tissue resection in humans have never been reported to facilitate cancer recurrence. The objective of the present research is to evaluate mammalian ECM as a novel approach to glioma therapy. **METHODS/STUDY POPULATION:** ECM hydrogels from porcine dermis, small intestine, and urinary bladder were produced as described previously. Primary glioma cells were graciously supplied by Drs. Nduka Amankulor and Johnathan Engh, and U-87 MG were ordered through ATCC. Cells were plated onto tissue culture plastic at ~60% confluence and allowed to attach for 24 hours before treatment. The saline-soluble fraction (SSF) of ECM was obtained by mixing lyophilized, comminuted ECM with 0.9% saline for 24 hours then filtering the resulting mixture through a 10 kDa molecular weight cutoff column. All assays and kits were followed according to the manufacturer's instructions. Cell viability was measured via MTT assay (Vybrant[®] MTT Cell Proliferation Assay, Invitrogen) and by live/dead staining (LIVE/DEAD[®] Cell Imaging Kit, Invitrogen). Time lapse videos were created by taking images every 20 minutes for 18 hours (phase-contrast) or every 10 minutes for 12 hours (darkfield). NucView reagent was ordered from Biotium. Temozolomide was ordered through Abmole. All in vivo work was conducted according to protocols approved by the University of Pittsburgh's IACUC office. **RESULTS/ANTICIPATED RESULTS:** ECM hydrogels derived from porcine dermis, small intestine, or urinary bladder all decreased the viability of primary glioma cells in vitro, with urinary bladder extracellular matrix (UBM) having the most dramatic effects. The SSF of UBM (UBM-SSF), devoid of the fibrillar, macromolecular components of ECM, was sufficient to recapitulate this detrimental effect upon neoplastic cells in vitro and was used for the remainder of the experiments described herein. In a cell viability assay normalized to the media treatment, non-neoplastic CHME5 and N1E-115 cells scored 103% and 114% after 48 hours when treated with UBM-SSF and 2 primary high-grade glioma cell types scored 17% and 30.5% with UBM-SSF ($n=2$). Phase-contrast time-lapse video showed CHME5 and HFF thriving in the presence of UBM-SSF for 18 hours while most primary glioma cells shriveled and died within this time. Darkfield time-lapse video of wells containing Nucview dye, fluorescent upon cleavage by active caspase-3, confirmed that within 12 hours most primary glioma cells underwent apoptosis while CHME5 and HFF did not. In culture with primary astrocytes, high grade primary glioma cells, and U-87 MG glioma cells for 24 hours, UBM-SSF was found to significantly increase the population of primary astrocytes compared with media ($p < 0.05$) while decreasing the 2 glioma cell types to approximately one-third as many cells as the media control ($p < 0.0001$). A dose-response of temozolomide from 0 to 10,000 μM showed that when treating 2 non-neoplastic cell types (CHME5 and HFF) and 2 types of primary glioma cell there was no difference in survivability at any concentration. Contrasted to this, a dose-response of UBM-SSF from 350 to 7000 $\mu\text{g}/\text{mL}$ showed that the non-neoplastic cells survived significantly better than the glioma cells at concentrations of 875 $\mu\text{g}/\text{mL}$ and upward ($p < 0.05$). In preliminary animal experiments, large primary glioma tumors in the flanks of athymic nude mice were resected and replaced with either UBM SSF or Matrigel (an ECM product of neoplastic cell origin). After 7 days the resection sites with UBM-SSF had little tumor regrowth if any compared with the dramatic recurrence seen in the Matrigel injection sites ($n=2$). In a separate survival study comparing PBS to UBM-SSF injections in the flank-resection model, all animals given PBS had to be sacrificed at 9, 11, and 11 days ($n=3$) whereas animals given UBM-SSF were sacrificed at 15, 24, and 39 days ($n=3$), indicating a moderate increase in survival due to the UBM-SSF. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Since the introduction of the pan-cytotoxic chemotherapeutic agent TMZ in 2005, the standard of care for patients with glioblastoma multiforme has not improved. These findings indicate that non-neoplastic ECM contains potent bioactive regulators capable of abrogating malignancy. Our in vitro data suggest these molecules appear to have no deleterious effect on non-neoplastic cells while specifically inducing apoptosis in glioma cells. Our in vivo data suggest that these molecules may be useful in delaying glioma recurrence, thus resulting in extended lifespan. Delivering soluble fractions of ECM to a tumor site may represent a novel approach to glioma therapy, sidestepping traditional cytotoxic therapies in favor of utilizing putative endogenous anti-tumor pathways.

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Feasibility, acceptability, and appropriateness of the menstrual cup for short-term non-surgical management of vesicovaginal fistula (VVF) among potential users and stakeholders

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OBJECTIVES/SPECIFIC AIMS: To examine how women with OF in Ghana develop strategies for coping in the absence of access to successful surgical repair. To assess the feasibility, acceptability, and appropriateness of an innovation to support coping among women with OF seeking care in a health facility in Ghana. To examine the perceived facilitators and barriers to implementation among additional OF stakeholders regarding the innovation. **METHODS/STUDY POPULATION:** This study uses a sequential exploratory mixed methods design. The population of study is women in Ghana living with obstetric fistula, as well as additional fistula stakeholders (programmers, policy makers, community leaders). To get an understanding of usual leakage, women carried out at baseline a pad test, where they wore a sanitary pad for 2 hours and leaked freely. We subtracted the dry pad weight from the wet pad weight to estimate urine leakage in mL. Then women inserted the cup for 2 hours and again wore a pad and urine leakage was estimated. Acceptability among women with vesicovaginal fistula was measured by questionnaire. Acceptability among additional stakeholders was examined by semistructured interview. Appropriateness was assessed among the user, additional stakeholders, and organizational setting. **RESULTS/ANTICIPATED RESULTS:** We observed a 61% mean reduction in leakage with the cup which was also perceived by cup users as a reduction in wetness. Notably, one participant who had 4 previous surgical attempts, experienced a 78% reduction in leakage. No adverse events attributable to use of the cup were observed, unlike some of the strategies women currently use to manage leakage. Acceptability was high as most women could easily insert, remove, and wear the cup over the 2-hour period and fistula stakeholders indicated the innovation content and complexity were acceptable. In community interviews, women shared various coping and self-care strategies to manage their leaking, other related impairments, and stigma. Women using the cup in the health facility expressed that it was useful. Additional stakeholders found the cup a low-cost, low-tech solution to supplement existing programs. Within the stakeholder interviews we heard that the cultural norms and existing activities of the potential implementation partners align with the innovation approach. Stakeholders revealed various implementation facilitators and barriers. The facilitators to implementation reported in the interviews were related to the intervention and organization characteristics in particular. Stakeholders perceived a relative advantage to self-management. Stakeholders had concerns regarding whether women would find the insertable device acceptable and appropriate—questioning whether potential users would have access to water, soap, and safe space to empty cup. **DISCUSSION/SIGNIFICANCE OF IMPACT:** The innovation is efficacious, acceptable, adds to current coping strategies, and fits within existing fistula programs. Stakeholders pre-implementation perceptions highlight the importance of partnerships and the need for an evidence base related to effectiveness, acceptability, and cost. Challenges to address include access to resources within these contexts (water, soap, and safe space) and development appropriate counseling message.

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Fecal bile acids, fecal short-chain fatty acids, and the intestinal microbiota in patients with irritable bowel syndrome (IBS) and control volunteers

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OBJECTIVES/SPECIFIC AIMS: Objectives and goals of this study will be to: (1) compare fecal microbiota and fecal organic acids in irritable bowel syndrome (IBS) patients and controls and (2) investigate the association between colonic transit and fecal microbiota in IBS patients and controls. **METHODS/STUDY POPULATION:** We propose an investigation of fecal organic acids, colonic transit and fecal microbiota in 36 IBS patients and 18 healthy controls. The target population will be adults ages 18–65 years meeting Rome IV criteria for IBS (both diarrhea- and constipation-predominant, IBS-D and IBS-C) and asymptomatic controls. Exclusion criteria are: (a) history of microscopic colitis, inflammatory bowel disease, celiac disease, visceral cancer, chronic infectious disease, immunodeficiency, uncontrolled thyroid disease, liver disease, or elevated AST/ALT $> 2.0 \times$ the upper limit of normal, (b) prior radiation therapy of the abdomen or abdominal surgeries with the exception of appendectomy or cholecystectomy > 6 months before study initiation, (c) ingestion of prescription, over the counter, or herbal medications affecting gastrointestinal transit or study interpretation within 6 months of study initiation for controls or within 2 days before study initiation for IBS patients, (d) pregnant females, (e) antibiotic usage within 3 months before study participation, (f) prebiotic or probiotic usage within the 2 weeks before study initiation, (g) tobacco users. Primary outcomes will be fecal bile acid excretion and profile, short-chain fatty acid excretion and profile, colonic transit, and fecal microbiota. Secondary outcomes will be stool characteristics based on responses to validated bowel diaries. Stool samples will be collected from participants during the last 2 days of a 4-day 100 g fat diet and split into 3 samples for fecal microbiota, SCFA, and bile acid analysis and

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.

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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.

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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.

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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 I). METHODS/STUDY POPULATION: Women with recurrent BV (≥ 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 I, 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.

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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