postmenopausal women. A total of 78 subjects completed the study, with 12 subjects dropping out due to non-compliance and medical reasons. Supplementation with fish oil attenuated the thrombin receptor PAR4-induced platelet aggregation, whereas primrose oil supplementation attenuated aggregation mediated by PAR4 or collagen. Supplementation with âµ-3 or âµ-6 fatty acids decreased platelet dense granule secretion and attenuated basal levels of integrin âºIIbÎ²3 activation. Post-washout following supplementation with primrose oil, the thrombin receptor PAR1-induced platelet aggregation was similarly attenuated. For either treatment, the observed effects post supplementation on dense granule secretion and basal integrin activation were sustained after the washout. DISCUSSION/SIGNIFICANCE: Postmenopausal women are at increased risk for a cardiovascular event due to platelet hyperactivity. This study indicates that supplementation with âµ-3 and âµ-6 fatty acids may offer significant protection for postmenopausal women against cardiovascular diseases and occlusive thrombotic events by reducing platelet reactivity.

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Identification of Trichomonas vaginalis 5-nitroimidazole resistance targets to inform future drug development

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OBJECTIVES/GOALS: 5-nitroimidazoles are the only FDA-approved medications for T. vaginalis treatment. Resistance has been observed in 5-10% of cases, but may be rising. We aimed to delineate mechanisms of resistance in isolates of T. vaginalis using transcriptome profiling of resistant and sensitive T. vaginalis isolates. METHODS/STUDY POPULATION: T. vaginalis isolates (4 metronidazole (MTZ)-resistant were grown in triplicate in Diamond's Trypticase-Yeast-Maltose medium. MTZ susceptibility testing confirmed MTZ MLCs of T. vaginalis isolates. Total RNA extraction was done using Trizol reagent (Invitrogen; Carlsbad; CA); according to the manufacturer's instructions. RNA sequencing (RNAseq) and bioinformatics analyses were performed to identify significantly differentially expressed genes (DEGs) in MTZ-resistant vs. sensitive isolates. Subsequent qPCR was performed to confirm and extend RNAseq data and gene targets related to 5-nitroimidazole resistance. RESULTS/ANTICIPATED RESULTS: RNAseq identified key DEGs in MTZ-resistant vs. sensitive isolates. DEGs from MTZ-resistant isolates included those involved in metabolic pathways relevant to 5-nitroimidazole resistance such as energy production (glycolytic enzymes) and oxygen-scavenging (thioredoxin). Other DEGs included those encoding transcription factors (MYB DNA-binding protein), ribosomal proteins (30S, 40S, 50S, 60S), protein kinases (CAMK, ser/thr, CMGC), Ankyrin repeat proteins, surface proteins (Surface antigen BspA-like) and various uncharacterized hypothetical proteins. RT-qPCR experiments confirmed reduced expression of genes encoding ferredoxin (drug activation) and flavin reductase 1 (oxygen scavenging) in MTZ-resistant T. vaginalis isolates as compared to MTZ-sensitive isolates. DISCUSSION/SIGNIFICANCE: In this study, we identified several DEGs in resistant T. vaginalis isolates. Further studies with large number of isolates representing a broad range of MTZ-susceptibility patterns are needed to identify genes that may represent new targets for future drug development.

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A CTS Team Approach to Modeling Migration and Suppression of CCR2+/CX3CR1+ Myeloid Cells in Glioblastoma

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OBJECTIVES/GOALS: Evaluate the migration and immune suppressive functions of CCR2+/CX3CR1+ myeloid-derived suppressor cells (MDSCs). Integrate experimental data and biologically relevant mathematical models of infiltrating MDSCs in the context of glioblastoma (GBM). METHODS/STUDY POPULATION: CCR2+/CX3CR1+ cells were enriched from bone marrow obtained from CCR2(+/RFP)/CX3CR1(+/GFP) glioma-bearing mice to evaluate their immune-suppressive phenotype and ability to migrate to CCL2 and CCL7. Fluorescent imaging and quantification were performed on a range of tumor sizes to acquire vasculature, tumor, T cell, and MDSC densities. A system of ordinary differential equations was constructed to represent the temporal dynamics of glioma cells, T cells, and MDSCs within the tumor microenvironment. The Approximate Bayesian Computation method was used to determine probability distributions of important parameters, such as the suppression rate of T cells by MDSCs. RESULTS/ANTICIPATED RESULTS: CCR2+/CX3CR1+ M-MDSCs isolated from the bone marrow of tumor-bearing mice suppress CD8+ T cell proliferation and IFNÎ³ production. CCR2+/CX3CR1+ cells migrate to recombinant and KR158B glioma sourced CCL2 and CCL7. Parameter values determined by the Approximate Bayesian Computation method agreed with parameter values from experimental data. This result further validated the structure and results of the mathematical model when performing computer simulations; thus, we can predict CCR2+/CX3CR1+ M-MDSC infiltration over time. DISCUSSION/SIGNIFICANCE: The immune-suppressive microenvironment in GBM contributes to poor outcomes despite standard of care. This study integrates biological and mathematical models to better understand infiltrating immune-suppressive cells, namely CCR2+/CX3CR1+ M-MDSCs. Future directions include modeling immunotherapies.

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Antibody function, antigenic target and glycans determine the transfer of herpes simplex virus (HSV) antibodies (Abs) from mothers to newborns and transfer is altered by SARS-CoV-2*

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OBJECTIVES/GOALS: Murine and clinical data suggest that antibody-dependent cellular cytotoxicity (ADCC) is associated with greater protection against disseminated neonatal HSV disease. To quantify the relative transfer of Abs with different functions and targets, we conducted a prospective study of mother-infant term and

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preterm dyads pre and during COVID-19 METHODS/STUDY POPULATION: Total and HSV lysate, glycoprotein D (gD) and glycoprotein B (gB)-specific IgG, IgG1 and IgG3 as well as HSV neutralizing Abs (nAbs) and ADCC were quantified in paired 3rd-trimester pregnant women and their newborns (cord) blood. Transfer ratios (TR) were defined as cord:maternal Ab levels. IgG1 and IgG3 subclass and gD or gB-specific Abs were isolated by column purification and glycan profiles were assessed by mass spectrometry. The study population included 21 term and 15 preterm dyads who were HSV-1 (+/- HSV-2) seropositive enrolled between 2018-2019 (pre-COVID) and 25 additional HSV-1 (+/- HSV-2) seropositive term dyads whose mothers were SARS-CoV-2 PCR and COVID Ab+ at delivery; 14 were asymptomatic and 11 had mild-moderate COVID disease. None of the mothers had active genital HSV lesions during delivery RESULTS/ANTICIPATED RESULTS: Anti-HSV IgG, IgG1 and IgG3 TR were higher in term vs. preterm dyads ($p<0.05$). The nAb TR was 2.4 in term vs. 0.8 in preterm ($p<0.001$) but the ADCC TR was < 1.0 for both. To determine if the latter reflected antigenic target, subclass or glycans, we enriched for gD and gB specific and IgG1 and IgG3 Abs. The gD Abs were IgG1 and had only neutralizing activity. In contrast, gB Abs were polyfunctional and included IgG1 and IgG3 but only the IgG1 Abs had ADCC activity. The gD Abs were enriched for glycans associated with an affinity for the neonatal Fc receptor (FcRn); gB Abs expressed glycans associated with both FcRn and FcÎ³RIIIa binding. There was no significant difference in total HSV-specific IgG TR in pre-COVID vs post-COVID dyads but the nAb TR was lower ($p=0.018$) and ADCC TR higher ($p<0.001$) in the COVID compared to pre-COVID cohort DISCUSSION/SIGNIFICANCE: HSV ADCC Abs, which may provide greater protection than nAbs against neonatal disease, transfer poorly particularly to preterm newborns. However, in the setting of SARS-CoV-2, the TR of HSV ADCC is significantly higher. This may reflect alterations in the placental architecture and/or glycan composition which is currently being investigated.

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Using team science to support outbreak management in a large urban region during the COVID-19 pandemic

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OBJECTIVES/GOALS: To describe how the UCLA Clinical and Translational Science Institute (CTSI) assembled and deployed a science team in support of a local jurisdictions effort to manage and control COVID-19 outbreaks in one of the nations largest metropolitan regions, Los Angeles County (LAC). METHODS/STUDY POPULATION: During the COVID-19 pandemic (2020-21), building an efficient data infrastructure to support outbreak management became a priority for the local health department. In response, the UCLA CTSI assembled a science team with expertise across the translational continuum: epidemiology, laboratory and microbiology, machine learning, health policy, medicine and clinical care, and community engagement. The team partnered with a new LAC Data Science Team to foster a collaborative learning environment for scientists and public health personnel, employing improvement and implementation science to help mitigate COVID-19 outbreaks in sectors including healthcare, skilled nursing facilities, and K-12 education. The goal was a public health workforce that is prepared to problem-solve complex, evolving outbreaks. RESULTS/ANTICIPATED RESULTS: The science team created a learning environment with data modeling and visualization, problem-based learning, and active knowledge and skills acquisition. First, control charts and time series methods were used to visualize COVID-19 data and find signals for action. Second, a series of 16 Grand Rounds offered interactive sessions on problem-solving of outbreak challenges in different sectors. Third, a biweekly Public Health Digest provided fieldworkers with the latest scientific studies on COVID-19. All three elements guided and empowered the workforce to implement timelier, efficient outbreak mitigation strategies in the field. The partnered team also identified barriers to adoption of selected new data and management techniques, revealing areas for further skill-building and data-driven leadership. DISCUSSION/SIGNIFICANCE: The UCLA CTSI science team offered a backbone science infrastructure for helping public health and other sector agencies manage COVID-19 outbreaks and mitigation. It showed promise in bringing and translating science into public health practice. It revealed future priorities for CTSI innovation and scientific support of public agencies.

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Development and implementation of research team: Lessons learned from conducting studies focusing on sleep and brain aging

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OBJECTIVES/GOALS: This poster summarizes the development and implementation of research exploring the relationship between sleep and brain health. METHODS/STUDY POPULATION: Three pilot studies and two secondary data analyses were conducted on 20 older adults with coronary artery disease and 30 older adults without major cardiovascular disease. They were recruited for 10 older adults with multiple chronic conditions. The study included interviews, magnetic resonance imaging, and sleep assessment of participants. Data were also gathered from two secondary sources on multiple chronic conditions, sleep, neuroimaging, cognition, and Alzheimers biomarkers. RESULTS/ANTICIPATED RESULTS: The multidisciplinary team was from nursing, medicine, cardiology, psychology, neuroscience, radiology, and data science to address the separate research aims. The pilot studies and secondary data analyses were successfully implemented. The University of Iowa Institute for Clinical and Translational Science, Center for Advancing Multimorbidity Science, and Iowa Neuroscience Consortium supported the collaboration. The teams have found that sleep and circadian rhythms

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