tool for assessing motor pathways in infants with early brain injury, highlighting its potential for clinical translation in neurodevelopmental disorders, and offering a pathway to improved care.

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Characterizing clinical predictors of metabolic syndrome associated with second-generation antipsychotics in pediatric populations

Nihal El Rouby, Lisa J Martin, Leah C Kottyan, Cindy A Prows, Namjou-Khales, Jeffrey A Welge, Nancy Crimmins, Jeffrey R Strawn and Melissa P DelBello
University of Cincinnati

OBJECTIVES/GOALS: Second-generation antipsychotics (SGA) are used to treat mental disorders in youth but are linked metabolic syndrome (MetS). Most data on prescribing practices and risk factors are from short-term studies (6–12 months). We aim to characterize prescribing and identify clinical and genetic predictors of MetS using electronic health records (EHR). METHODS/STUDY POPULATION: EHR data were extracted from Cincinnati Children's Hospital Medical Center (CCHMC) for patients aged ≤21 years prescribed SGAs from 7/1/2009 and 7/1/2024, identifying prescribing prevalence. Next steps are to create an SGA-MetS case–control dataset 8 weeks after an SGA prescription. A case will be defined by meeting 3 of 5 criteria: 1) BMI ≥95th percentile for age/sex; 2) fasting glucose ≥100 mg/dL or use of anti-diabetics; 3) triglycerides ≥110 mg/dL; 4) HDL-C ≤40 mg/dL; 5) systolic/diastolic BP ≥90th percentile for age/sex or use of antihypertensives. The prevalence of SGA-MetS will be calculated by dividing SGA-MetS cases by total SGA users. Logistic regression will identify clinical predictors of MetS, and we will evaluate the association of polygenic risk scores (PRS) of BMI and type 2 diabetes with SGA-MetS risk. RESULTS/ANTICIPATED RESULTS: Our preliminary analysis identified 30,076 patients who were prescribed SGAs (mean age 12 years, SD = 4; 58.8% female; n = 17685). Most self-identified as non-Hispanic (95%, n = 28,595) and of White race (76%; n = 22,935), with 18.5% self-identifying as Black or African American (n = 5,579). The most commonly prescribed SGAs were risperidone (n = 12,382, 41.1%), aripiprazole (n = 9,847, 32.7%), and quetiapine (n = 5,263, 17.5%), with much lower prescribing rates of other SGA known of their low risk of MetS (e.g., ziprasidone 5.5%, lurasidone 1.4%, paliperidone (n = 316, 1.1%), or others cariprazine (n = 72), asenapine (n = 43), brexipiprazole (n = 39), iloperidone (n = 24), and clozapine (n = 20). DISCUSSION/SIGNIFICANCE OF IMPACT: Our analyses found that risperidone, quetiapine, and aripiprazole were the most prescribed SGA, with risperidone/quetiapine linked to a higher risk of MetS. We will present ongoing work identifying risk factors for SGA-MetS and examining the association with PRS. Our work has the potential to identify high-risk patients for personalized treatment.

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DNA targeting autoantibody for brain tumor therapy*

Olivia Turk and James E. Hansen
Yale School of Medicine

OBJECTIVES/GOALS: Nucleoside transport by ENT2 facilitates transit of the lupus anti-DNA autoantibody Deoxymab into cells and across the blood–brain barrier into brain tumors. This work examines the Deoxymab-nucleoside interactions that contribute to membrane crossing and apply them in brain tumor therapeutics. METHODS/STUDY POPULATION: Deoxymab interactions with individual nucleosides, nucleobases, and pentose sugars are examined by surface plasma resonance (SPR) and cell penetration assays in a panel of cell lines including glioblastoma, breast cancer, and normal breast epithelial cells. Deoxymab-conjugated gold nanoparticles are generated and tested for binding to normal human astrocytes and glioma cells, and the impact of supplemental nucleosides on this binding is determined. Deoxymab-gold nanoparticles are tested for brain tumor localization by systemic and local administration in mice bearing orthotopic glioblastoma brain tumors and enhancement of laser interstitial thermal therapy (LITT) examined. RESULTS/ANTICIPATED RESULTS: Individual nucleosides significantly increase the efficiency of cell penetration by Deoxymab in all cell lines tested. In contrast, component nucleobases and pentose sugars significantly suppress the uptake of the autoantibody into cells. Deoxymab-conjugated gold nanoparticles bind DNA in vitro and to astrocytes in culture and are anticipated will enhance the efficacy if LITT in vivo by associating with DNA released by necrotic tumors and/or by locally administered nucleosides in brain tumor environments and subsequently act as heat sink to amplify LITT impact. DISCUSSION/SIGNIFICANCE OF IMPACT: Deoxymab is a DNA-targeting, cell-penetrating autoantibody. These findings establish nucleosides as the components of DNA that promote autoantibody membrane crossing through ENT2 activity and indicate potential for use of Deoxymab-gold nanoparticles in combination with LITT for brain tumor therapy.

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The genetic risk assessment with mobile mammography (GRAMM) project: Providing genetic counseling referrals in tandem with mobile mammography for at-risk Black women

Versha Pleasant, Kiyah Mills, Audrey Widner, Kara J. Milliron and Sofia Merajver
University of Michigan

OBJECTIVES/GOALS: The overarching goal of the GRAMM study is to address racial health disparities by increasing access to genetic counseling and testing among the Black community. Specific objectives are to determine patient acceptability of risk assessment at time of mammography and to evaluate subsequent access to and uptake of genetic counseling and testing. METHODS/STUDY POPULATION: All women presenting for screening mammography at the Ypsilanti Health Center under the University of Michigan were invited to enroll. After providing written informed consent, study participants entered family cancer and personal health information in the InheRET software tool which links to the National Comprehensive Cancer Network genetic testing guidelines. Upon completion, each participant was informed immediately if they did or did not meet the criteria to meet with a genetic counselor. For those who met the criteria, referral to genetic counseling was provided. All enrollees were invited to complete a post-assessment survey on acceptability of the service and genetics knowledge. Patients will be followed over time for completion of genetic counseling and testing. The study was approved by the Umich IRB. RESULTS/

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ANTICIPATED RESULTS: As of 10/18/24, a total of 53 were enrolled, with 52 eligible for the study and were between the ages of 30–75 years. 51 identified as women and 1 identified as nonbinary. 21 (40.4%) identified as Black, 30 (57.7%) identified as White, 2 (3.8%) identified as Hispanic, and 1 (1.9%) identified as mixed race. Of the total enrolled, 25 (48.1%) met criteria to meet with a genetic counselor. Twelve (23.1%) have been scheduled to with meet with a genetic counselor and 2 (3.8%) of this group completed their appointment, but did not pursue genetic testing. 28 (53.8%) completed the survey and reported that they were satisfied with the service. Of the 16 people who screened positive and completed the survey, all 16 (100%) stated that they intended on proceeding with testing. Our study is still ongoing. DISCUSSION/SIGNIFICANCE OF IMPACT: While this model has demonstrated acceptability so far, there are still possible barriers to genetic counseling and testing after the referral has been provided that need to be explored. However, this approach could provide a novel framework for combining risk assessment with screening mammography for all women nationwide.

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Sarcopenia severity in males between the ages of 3 to 20 years old with duchenne muscular dystrophy (DMD) in Puerto Rico

Edwardo Ramos and Jose G Conde
School of Medicine University of Puerto Rico

OBJECTIVES/GOALS: Objectives/Goals (300 characters): Sarcopenia is a progressive skeletal muscle disorder associated with adverse outcomes. There is a gab of having objective measures upon performing interventions in patients with muscular dystrophies. The object of the present study is to describe the severity of sarcopenia in DMD patients in Puerto Rico. METHODS/STUDY POPULATION: Methods/Study Population (700 characters): Forty to 30 patients with DMD who are followed in MDA Care Center in the "Instituto De Rehabilitacion del Caribe." Diagnosis will be confirmed with genetic testing and/or muscle biopsy. Lean muscle mass will be measured with a Whole Body Dexa (WBD) in a Nuclear Medicine Lab. Hand grip, elbow flexor, and knee extensor muscles strength will be measures with an isometric dynamometer. Patients' functionality will done using the North Star Ambulatory Assessment scale and Brook and Vignos scales, which have been validated for patients with DMD and neuromuscular disease respectively. Correlations will be made with lean body mass (independent variable) and muscle strength and functionality (dependent variable). RESULTS/ANTICIPATED RESULTS: Results/Anticipated Results (700 characters): We expect to find severe sarcopenia in patients with DMD in PR and that it will be more severe with older age. There will be a direct correlation between lean muscle mass and muscle strength, and functionality in DMD patients. DISCUSSION/SIGNIFICANCE OF IMPACT: Discussion/Significance of Impact (300 characters): The findings of our study can help us to explore the possibility that Whole Body DEXA can serve as a potential biomarker for future studies since there is a need to develop noninvasive biomarkers that correlate with disease progression and interventions in DMD patients.

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Intestinal CD4:CD8 ratio and systemic inflammatory parameters in suppressed HIV-1 infection

Francesca Cossarini, Pablo Canales-Herrerias, Divya Jha, Alexandra E. Livanos, Michael Tankelevich and Saurabh Mehandru
Icahn School of Medicine at Mount Sinai

OBJECTIVES/GOALS: To determine the heterogeneity in CD4:CD8 ratio in a well-characterized cohort of PWH and to investigate the predictors of intestinal CD4:CD8 ratio reconstitution (CD4:CD8>1) and its impact on systemic inflammation. METHODS/STUDY POPULATION: We enrolled 52 PWH on ART and with peripheral HIV-RNA RESULTS/ANTICIPATED RESULTS: PWH had a lower CD4:CD8 ratio both in the peripheral blood [p1. This subset of PWH was more likely female (62% vs. 38%, p = 0.0158), diagnosed with HIV for a longer time [p = 0.0347] have longer duration of most recent viral suppression [p = 0.0365] higher CD4+ T cells at enrollment [p = 0.0262] and higher CD4+ T cell nadir. Multiple logistic regression showed that duration of HIV infection [OR 1.13 (95% C.I. 1.02–1.3)] and CD4 = T cell nadir[OR 1.01 (95% C.I. 1.001–1.016)] were associated with colonic CD4:CD8 >1. Colonic CD4:CD8 ratio partially correlated with the peripheral blood CD4:CD8 ratio (r = 0.274, p = 0.068) and with the pro-inflammatory cytokines IL-20 (r = -0.413, p = 0.036) and SLAMF-1 (r = -0.329, p = 0.074). DISCUSSION/SIGNIFICANCE OF IMPACT: In PWH, CD4:CD8 ratio

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Elucidating the epigenetic regulation of estrogen receptor-positive breast cancer cells by parathyroid hormone-related protein (PTHrP)

Madeline Searcy, Jeremy Kane, Bradley Ludington, Michael Phan and Rachelle Johnson
Vanderbilt University Medical Center

OBJECTIVES/GOALS: We have shown that parathyroid hormone-related protein (PTHrP) is enriched at the LIFR promoter in breast cancer cells and inhibits the expression of dormancy-associated genes including LIFR. The objective of this study is to define where all PTHrP binds DNA and identify pathways that are regulated by PTHrP that promote breast cancer colonization of the bone. METHODS/STUDY POPULATION: In this study, we use human estrogen receptor-positive MCF7 breast cancer cells which we and others have reported lie dormant in the bone. MCF7 cells were engineered to express either PTHrP with an HA-tag (MCF7P), or a vector control (MCF7V). We use Cleavage Under Targets and Release Using Nuclease (CUT&RUN), a method of mapping protein-DNA interactions, to define where PTHrP binds DNA. Here, an HA-specific antibody identifies regions of DNA that are bound to PTHrP in MCF7P cells compared to MCFV cells. Next, we perform DNA sequencing and gene set enrichment analysis (GSEA) on genes identified by CUT&RUN to identify pathways that are regulated by PTHrP. These experiments will determine how PTHrP regulates dormancy and breast cancer colonization in the bone. RESULTS/ANTICIPATED RESULTS: We completed IgG (-control),

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