glioma and GNR-labeled HSC bio-distribution will be measured after ACT and correlated with survival outcomes. RESULTS/ANTICIPATED RESULTS: We have demonstrated that GNRs are readily taken up by HSCs within 30 minutes, and retained within intracellular compartments, via TPL. Incubation of GNRs with HSCs did not significantly alter cell viability or differentiation, supporting the GNR's favorable biosafety profile. Colony-forming unit assays revealed that GNR incubation did not significantly disrupt the total number of colonies formed and qualitatively, colonies did not demonstrate significant lineage differences. GNR-labeled HSCs demonstrated significant reconstitution after myeloablative total body irradiation in mice. We expect that GNR-labeled HSCs will distribute to the glioma microenvironment and draining lymph nodes, positively correlating with long-term survival after ACT. DISCUSSION/SIGNIFICANCE OF IMPACT: GNRs harbored high biosafety and feasibility for tracking HSC migration after ACT. We seek to translate this theranostic tool into the current first-in-human clinical trials at our institution for patients diagnosed with neuroblastoma and diffuse intrinsic pontine glioma to improve immunotherapies against brain malignancies.

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Perinatal opioid exposure compromises placental structure and alters immune function at the maternal–fetal interface†

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OBJECTIVES/GOALS: Opioid use disorder (OUD) in pregnancy and its implications on the maternal-fetal interface has been relatively understudied. Here, we aimed to uncover the impact of maternal OUD on placental structure, function, and inflammatory responses and further stratified our findings by maternal hepatitis C (HCV) infection. METHODS/STUDY POPULATION: To address this knowledge gap, we collected placental tissue from healthy pregnancies (control) and those with opioid use disorder with and without maternal HCV infection. First, placental development was assessed by gross and histological examination of the placenta. Immune cells were then isolated from decidua (maternal) and chorionic villous (fetal) placental tissues, and the frequency and phenotype of immune subsets were determined by flow cytometry. Markers of inflammation, placental perfusion, growth factors, tissue remodeling, and vascularization were measured in placental tissue homogenate by multiplex Luminex assay. Finally, gene expression alterations in placental architecture were assessed by Visium spatial transcriptomics, integrating transcriptomic data with spatial information. RESULTS/ANTICIPATED RESULTS: Our results indicate that maternal OUD impairs placental perfusion/development and is accompanied by increased markers of inflammation in the decidua (IL-1Ra, IL-2, IL-18, IP-10, MIP-1β, and TNFα) and villous (IL-6 and IL-8). Furthermore, markers of angiogenesis and placental development are altered in the decidua, including increased EGF and IL-6Ra, but decreased FLT-1, FLT-4, and bFGF. The abundance of placental immune cells is varied with OUD/HCV, including decreased frequencies of decidual macrophages and NK cells, critical for blood supply to the fetus, and increased abundance of infiltrating maternal macrophages in fetal chorionic villous. Finally, spatial transcriptomics revealed aberrant infiltration of activated immune cells and modified processes associated with inflammation and angiogenesis. DISCUSSION/SIGNIFICANCE OF IMPACT: Altogether, these findings suggest a profound impact of maternal OUD with and without maternal HCV infection on the structure, function, and immune landscape of the maternal–fetal interface that can alter fetal development and maturation.

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Burden of trauma in incident Parkinson's disease patients

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OBJECTIVES/GOALS: We investigated the risk of trauma in the form of fractures and traumatic brain injuries (TBIs) among Medicare beneficiaries with incident Parkinson's disease (PD) age ≥67 compared to population-based controls. Secondarily, we examined the risk of death following a fracture in PD cases compared to controls. METHODS/STUDY POPULATION: We identified incident PD cases (N = 94,317) within a population-based sample of 2017 Medicare beneficiaries. Controls (N = 471,585) were matched 5:1 on month and year. We obtained claims data from 2017 to 2019 to follow cases and controls to identify new fractures treated in a hospital. Our primary outcome was any fracture. We also considered fracture type and TBI. We compared frailty level between cases and controls. We used logistic regression models to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between trauma and PD after adjusting for the following covariates: selected medical comorbidities, age, sex, race/ethnicity, smoking, and use of care. We used Cox regression to estimate hazard ratios (HRs) and 95% CI for trauma in cases compared to controls using the same covariates. RESULTS/ANTICIPATED RESULTS: Compared to controls, PD patients who developed a fracture were more likely to have a history of falls (OR = 2.20, 95% CI 2.08–2.34) and difficulties in walking (OR = 2.66, 95% CI 2.50–2.82). Compared to controls with a fracture, PD patients with a fracture were more likely to be moderately frail (OR = 1.43, 95% CI 1.25–1.64). PD cases had a higher risk of all fracture types, including hip (OR = 1.93, 95% CI 1.85, 2.01), spine (OR = 1.90, 95% CI 1.79, 2.02), upper extremity (OR = 1.69, 95% CI 1.58–1.80), and other traumas such as a TBI (OR = 2.14, 95% CI 1.88–2.43). PD patients had greater mortality following a fracture (HR = 1.18, 95% CI 1.13–1.24) than controls. DISCUSSION/SIGNIFICANCE OF IMPACT: The burden of trauma in the first

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two years immediately after PD diagnosis is high and warrants the initiation of early fall and fracture prevention strategies, in addition to aggressive treatment of PD symptoms by all providers caring for patients with PD.

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Positive SARS-CoV-2 symptomatology despite persistently negative molecular testing: Insights from a Multicenter Household Transmission Study

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OBJECTIVES/GOALS: We describe the prevalence of individuals with household exposure to SARS-CoV-2, who subsequently report symptoms consistent with COVID-19, while having PCR results persistently negative for SARS-CoV-2 (S[+]/P[-]). We assess whether paired serology can assist in identifying the true infection status of such individuals. METHODS/STUDY POPULATION: In a multicenter household transmission study, index patients with SARS-CoV-2 were identified and enrolled together with their household contacts within 1 week of index's illness onset. For 10 consecutive days, enrolled individuals provided daily symptom diaries and nasal specimens for polymerase chain reaction (PCR). Contacts were categorized into 4 groups based on presence of symptoms (S[+/-]) and PCR positivity (P[+/-]). Acute and convalescent blood specimens from these individuals (30 days apart) were subjected to quantitative serologic analysis for SARS-CoV-2 anti-nucleocapsid, spike, and receptor-binding domain antibodies. The antibody change in S[+]/P[-] individuals was assessed by thresholds derived from receiver operating characteristic (ROC) analysis of S[+]/P[+] (infected) versusS[-]/P[-] (uninfected). RESULTS/ANTICIPATED RESULTS: Among 1,433 contacts, 67% had ≥1 SARS-CoV-2 PCR[+] result, while 33% remained PCR[-]. Among the latter, 55% (n = 263) reported symptoms for at least 1 day, most commonly congestion (63%), fatigue (63%), headache (62%), cough (59%), and sore throat (50%). A history of both previous infection and vaccination was present in 37% of S[+]/P[-] individuals, 38% of S[-]/P[-], and 21% of S[+]/P[+] ($P<0.05$). Vaccination alone was present in 37%, 41%, and 52%, respectively. ROC analyses of paired serologic testing of S[+]/P[+] (n = 354) vs. S[-]/P[-] (n = 103) individuals found anti-nucleocapsid data had the highest area under the curve (0.87). Based on the 30-day antibody change, 6.9% of S[+]/P[-] individuals demonstrated an increased convalescent antibody signal, although a similar seroresponse in 7.8% of the S[-]/P[-] group was observed. DISCUSSION/SIGNIFICANCE OF IMPACT: Reporting respiratory symptoms was common among household contacts with persistent PCR[-] results. Paired serology analyses found similar seroresponses between S[+]/P[-] and S[-]/P[-] individuals. The symptomatic-but-PCR-negative phenomenon, while frequent, is unlikely attributable to true SARS-CoV-2 infections that go missed by PCR.

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Implementation of an analytic resource navigation process at an Academic Medical Center

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OBJECTIVES/GOALS: In 2018, a novel analytic resource navigation process was developed at Duke University to connect potential collaborators, leverage resources, and foster a community of quantitative researchers and scientists. We provide information about how this process works along with guidance for academic medical centers to develop similar initiatives. METHODS/STUDY POPULATION: Quantitative and qualitative scientists with expertise in data science, biostatistics, epidemiology, and related fields play a critical role in data collection, study design, analysis, interpretation, and implementation. The analytic resource navigation process connects researchers with quantitative scientists and relies on strong institutional knowledge of methodological expertise, understanding of research goals, educating researchers, and ongoing evaluation to understand unmet needs. University staff serve as navigators to help researchers identify the needed expertise, find potential collaborators, and track outcomes. Duke University's tracking system for this navigation process, implemented in 2019, underwent a nearly five-year evaluation (November 2019 – September 2024). RESULTS/ANTICIPATED RESULTS: In the nearly five-year evaluation of the process, 1247 requests from 813 unique researchers were navigated with a success rate of 93.8%. A total of 323 requests (256 unique researchers) were navigated in year 1, 285 requests (239 unique researchers) in year 2, 210 requests (179 unique researchers) in year 3, and 247 requests (192 unique researchers) in year 4. In the current year (partial year 5, 11/1/2023 – 9/18/2024), 182 requests have been navigated (159 unique researchers). Unsuccessful linkages occurred in 35 requests (2.8%) and 42 requests (3.4%) were withdrawn. Among the cases of unsuccessful navigation, 26 failed due to effort (e.g., insufficient effort available to meet the researcher's deadline), 2 failed due to lack of expertise at the institution, and 4 failed due to a lack of sufficient funding. DISCUSSION/SIGNIFICANCE OF IMPACT: The navigation process provides a critical resource for researchers who need to develop collaborations and a method for institutions to understand collaboration needs. Implementation requires training knowledgeable navigators, maintaining updated information about quantitative and qualitative methodologists, and institutional support.

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Single-cell comparative analysis reveals a similar regulatory subpopulation in white and brown adipocyte precursors

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OBJECTIVES/GOALS: The goal of this study is to resolve the complexity of the adipose precursor cells and identify potential therapeutic targets/mechanism to treat obesity, diabetes, cancer cachexia, and

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