multivariate logistic regression models to identify predictors of incident comorbidity within 12 months of COVID-19. RESULTS/ANTICIPATED RESULTS: o Previous work demonstrated that in PLWH, age and non-AIDS comorbidities, but not HIV-related factors, were associated with hospitalization for COVID-19 in a dose dependent fashion.18 We anticipate that rate of incident comorbidities will be significantly higher in PLWH after COVID-19 compared to PLWH without a history of COVID-19. We also expect that pre-existing comorbidities including obesity and cardiovascular disease, male sex, Black race, and older age are associated with higher incidence of post-COVID-19 comorbidities in PLWH. When stratifying by organ system, we also anticipate that prior comorbidities of an organ system will predispose patients to later complications of that same system. DISCUSSION/SIGNIFICANCE: By understanding the incidence and risk factors associated with developing post-COVID-19 comorbidities, we can improve guidelines for treatment of groups experiencing the disproportionate impact of co-infection with HIV and SARS-CoV-2.

479

Insomnia and Depression Trajectories in Women with and without Breast Cancer: Protective Effects of Satisfying Relationships

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OBJECTIVES/GOALS: Breast cancer survivors have a high risk for chronic disease and early mortality, especially if their psychological and physical symptoms persist beyond treatment. We compared survivors'and noncancer patient controls'health trajectories. We also examined how their relationship satisfactionâ€"a key health determinantâ€"impacted their health. METHODS/STUDY POPULATION: In this longitudinal study, participants were women who were married/domestic partners with an initial suggestive test of cancer identified at cancer clinics. After follow-up testing, women received either a malignant diagnosis (cancer survivors; n=139, stages 0–IIIC) or benign diagnosis (noncancer patient controls; n=69). Breast cancer survivors completed a baseline visit prior to beginning cancer treatment and two follow-up visits 6 and 18 months after treatment ended (surgery, radiation, or chemotherapy, whichever came last); noncancer patient controls completed visits within a comparable timeframe. At each visit, all women completed self-report questionnaires assessing their relationship satisfaction, insomnia, and depressive symptoms. RESULTS/ANTICIPATED RESULTS: We used mixed models and adjusted for participant age, comorbidities, cancer treatment and stage, BMI, and menopause status. At the pre-treatment visit, cancer survivors reported greater depressive symptoms than noncancer patient controls. Cancer survivors'depressive symptoms also decreased over time and were higher before treatment than at the 6- and 18-month post-treatment visits. Insomnia in cancer survivors, but not noncancer patient controls, decreased over time: insomnia was higher at the pre-treatment and 6-months post-treatment visits relative to the 18-month post-treatment visit. Survivors, but not noncancer patient controls, had lower depressive symptoms and insomnia at visits when they reported higher satisfaction than at visits when they reported lower satisfaction. DISCUSSION/SIGNIFICANCE: Cancer survivors had poorer psychological health than those without cancer before treatment, but survivors'psychological and physical health improved after finishing treatment. Survivors'satisfying relationships predicted better psychological and physical health, demonstrating the notable health benefits of survivors'relationships.

480

Integrating a Research Ethics Program within an Academic Health Science Center

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OBJECTIVES/GOALS: Research ethics services are critical to the clinical, research, and educational missions of an academic health science center. Our ethics program aims to develop a culture where investigators are as intellectually engaged in ethical issues of scientific integrity as they are in study design, data collection, and implementation. METHODS/STUDY POPULATION: This descriptive analysis depicts the historical development, from 2010 to 2022, of our research ethics program as an exemplar of ethics integration into the research enterprise of an academic health science center that engages in translational research. In this culture, clinicians, translational researchers and their scientific peers, research participants, and community members become involved in ethics investigation, deliberation, and innovation. RESULTS/ANTICIPATED RESULTS: There are four pillars to our research ethics program: 1) research ethics consultation service, which fosters the development of ethical best practices and standards for the practice of translational research; 2) education, which provides customized training and educational opportunities in research ethics to diverse stakeholders; 3) leadership, through collaboration and partnerships; 4) scholarly engagement, in the pursuit of innovative ethics research and professional development. Through these initiatives we can engage a broad constituency of stakeholders, become an integral component of research oversight, engage as active participants in the research enterprise, and have a critical role in guiding institutional culture. DISCUSSION/SIGNIFICANCE: The integration of our ethics program mirrors the translational science continuum which promotes the multidirectional flow of ideas among ethics consultants, laboratory/clinical scientists, implementation researchers and the community.

481

Interactions between buprenorphine and norbuprenorphine in neonatal opioid withdrawal syndrome*

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OBJECTIVES/GOALS: Buprenorphine (BUP) is used for opioid use disorder during pregnancy but causes neonatal opioid withdrawal syndrome (NOWS). The goal of this study was to determine the contribution of the active metabolite, norbuprenorphine (NorBUP), to the development of NOWS when the parent drug, BUP, is administered during pregnancy. METHODS/STUDY POPULATION: Subcutaneously implanted osmotic minipumps delivered BUP (0, 0.01, 0.1 or 1 mg/kg/day) ± NorBUP (1 mg/kg/day) to pregnant Long-Evans rats from gestation day 9 until after delivery. NOWS was measured between 3 and 12 hours after delivery. Withdrawal was precipitated by an intraperitoneal injection of a mu opioid

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receptor antagonist naltrexone (NTX; 0, 1 or 10 mg/kg), and movement duration (MD; a validated proxy for NOWS) was measured using Noldus Ethovision. Concentrations of BUP, NorBUP, and their glucuronide conjugates in the brains of neonatal littermates not undergoing withdrawal testing were determined using LC/MS/MS. Two-way ANOVA and multiple linear regression analyses tested for interactions between BUP and NorBUP on MD and related brain concentrations to MD, respectively. RESULTS/ANTICIPATED RESULTS: There was no interaction effect between BUP and NorBUP on MD for either sex or at any dose of naltrexone. In females, but not males, BUP (1 mg/kg/day) significantly increased NorBUP-induced MD by 58% following an injection with 1 mg/kg NTX. A multiple linear regression model that included BUP and NorBUP brain concentrations as predictors of MD was significant and well-fitting [FEMALES: $F(2, 40) = 23.97$, $P < .0001$, adj $R2 = 0.52$; MALES: $F(2, 40) = 5.84$, $P = .0059$, adj $R2 = 0.19$]. There was a differential contribution of NorBUP brain concentrations to MD based on sex. The partial regression coefficient for NorBUP was 51.34 ($p < .0001$) for females and 19.21 ($p = 0.093$) for males. The partial regression coefficient for BUP was similar for females and males (FEMALES:βBUP = 10.62, $p = .0017$; MALES:βBUP = 11.38, $p = .009$). DISCUSSION/SIGNIFICANCE: We show for the first time a differential contribution of NorBUP to BUP-associated NOWS in each sex, suggesting sex differences in NorBUP susceptibility and implicating that treatment strategies reducing prenatal NorBUP exposure may be more effective for females than males.

485

Modeling gastric mucus layer physiology using human organoids

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OBJECTIVES/GOALS: Our goal is to explore the extent to which organoids can serve as models for the protective mechanisms of the stomach–the mucus barrier and the pH gradient across it. We aim to first optimize and validate an organoid-based model of the gastric mucus layer, and then define the cellular mechanisms by which the gastric pH gradient is maintained across it. METHODS/STUDY POPULATION: We have developed a method for the in vitro engineering of gastric mucus by growing epithelial cells at the air-liquid interface (ALI). We use microrheology with fluorescent microspheres to define and compare the biophysical and viscoelastic properties of our lab-grown mucus to those of native mucus. We will perform CryoFE-SEM to compare the internal heterogeneity of our lab-grown mucus to fresh mucus obtained from patient tissue. For our mechanistic studies, we will use a pH-sensitive dye (methyl red) to assess the ability of our lab-grown mucus to maintain an artificial pH gradient in a microfluidic device. Next, we will use a pH microelectrode to measure proton flux through our mucus in vitro, investigating the potential for a physiological gradient in both 2D and 3D organoid models. RESULTS/ANTICIPATED RESULTS: Here we show that gastric organoids and their corresponding epithelial monolayers produce a mucus gel that does indeed mimic in vivo functions. Immunohistochemical staining, electron microscopy, microrheology, and particle tracking analyses revealed that our gastric organoid mucus is viscoelastic and structurally heterogeneous–both properties that are crucial to the stomach's mucosal first line of defense. Mechanically similar mucus was also engineered using two-dimensional air-liquid interface cultures of the same epithelia. Lastly, live confocal imaging revealed that H. pylori motility–an important virulence factor–was drastically hindered by our lab- grown mucus. DISCUSSION/SIGNIFICANCE: We describe a novel method for the in vitro engineering of gastric mucus and highlight biophysical properties that contribute to our stomach's defense against pathogens. This work will lead to an improved understanding of gastric physiology and may contribute to the development of novel drug delivery systems to tackle diseases of the gastric mucosa.

486

Molecular Mechanisms of Type II Spiral Ganglion Neuron Development

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OBJECTIVES/GOALS: 30,000,000 people in the U.S. have hearing loss, negatively impacting quality of life and work. Understanding auditory axon guidance for spiral ganglia neurons (SGNs) will aid development of new therapies. I study role of Eph/Ephrin signaling in mediating type II SGN turning events, and how planar cell polarity (PCP) signaling modulates this process. METHODS/STUDY POPULATION: This quantitative study was conducted on Efna3 and Vangl2 null mice possessing Neurog1CreERT2 and R26RtdTomato mutations. Spontaneous Cre activity within the Neurogenin 1 CreERT2 line causes recombination and expression of fluorescent Rosa26 Reporter (R26R)tdTomato in a restricted number of SGNs, including type IIs. Together these lines permit SGN sparse labeling. Bulk-labeling was used for Efna3;Vangl2 double knockout (DKO) mutants. Immunostaining and confocal imaging was used to analyze dsRed in Efna3; Vangl2 and NF-200 in DKOs to quantify type II SGN turning. In combination, 3D rendering in Imaris software was used to quantify type II SGN turning, branching and other growth and navigation characteristics. 5-6 cochleae per genotype were analyzed and compared by t-test to wildtype controls. RESULTS/ANTICIPATED RESULTS: EPHRIN-A3 is expressed on the membranes of outer pillar and Deiters'cells of the cochlear epithelium. Efna3 nulls showed a small rise in type II SGNs incorrectly turning toward the apex at an error frequency of 16.9% compared to controls (n=6; p=0.05). Efna3 nulls had reduced branch number/fiber compared to controls, 4.14 and 7.22, respectively (n=129; p DISCUSSION/SIGNIFICANCE: Our results suggest that Eph/Ephrin signaling acts parallel of PCP signaling to mediate type II SGN guidance during development. The clinical implications of these findings are that therapeutics targeting EPHRIN-A3 and/or VANGL2 in this pathway could stimulate new outer hair cell innervation by type II SGNs following auditory damage.

489

Nasal-derived Extracellular Vesicles (EVs) carry a cargo of antiviral and immunomodulatory molecules

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OBJECTIVES/GOALS: The goals of this project are to: i) investigate the cargo such as immune mediators (cytokines) and small non

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