

autologous activated T-cells in a dose-dependent manner. **DISCUSSION/SIGNIFICANCE OF IMPACT:** In this cross-sectional study of patients of the UT Southwestern Cutaneous Lupus Registry, we observed differences in the levels of MDSCs among PBMCs of CLE patients versus healthy controls. CLE patients had significantly higher levels of MDSCs, which could be explained by the presence of an inflammatory state in this group. Furthermore, CLE MDSCs were able to suppress autologous T cells, showing that these cells are functionally patent in CLE blood. Their up-regulation in CLE blood may represent the body's response to limiting disease severity, since most patients had mild disease activity.

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CYP2C19*2 and PON1 Q192R polymorphisms are associated with platelet reactivity to clopidogrel in Puerto Rican Hispanics with cardiovascular disease

Dagmar F. H. Suarez, Mariana R. Botton, Stuart A. Scott, Matthew I. Tomey, Kyle Melin, Angel Lopez-Candales, Jessica Y. Renta and Jorge Duconge
Icahn School of Medicine at Mount Sinai

OBJECTIVES/SPECIFIC AIMS: High on-treatment platelet reactivity (HTPR) with clopidogrel imparts an increased risk for ischemic events in adults with coronary artery disease. Although more potent antiplatelet agents are available, clopidogrel remains the most commonly used P2Y₁₂ inhibitor in Puerto Rico. Platelet reactivity varies with ethnicity and is influenced by both clinical and genetic variables; however, no clopidogrel pharmacogenetic studies with Puerto Rican patients have been reported. Therefore, we sought to identify clinical and genetic determinants of on-treatment platelet reactivity in a cohort of Puerto Rican patients with cardiovascular disease. **METHODS/STUDY POPULATION:** We performed a retrospective study of 111 Puerto Rican patients on 75 mg/day maintenance dose of clopidogrel. Patients were allocated into 2 groups: Group I, without HTPR; and Group II, with HTPR. Clinical data was obtained from the medical record. Platelet function was measured ex vivo using the VerifyNow[®] P2Y₁₂ assay and HTPR was defined as P2Y₁₂ reaction units (PRU) ≥ 230 . Genotyping of CYP2C19, ABCB1, PON1, PY2R12, B4GALT2, CES1, and PEAR1 was performed using Taqman[®] Genotyping Assays. **RESULTS/ANTICIPATED RESULTS:** The mean PRU across the cohort was 203 ± 61 PRU (range, 8–324), and 42 (38%) patients had HTPR. One in four individuals carried at least 1 copy of the CYP2C19*2 variant allele. Hematocrit and PON1 p.Q192R variant were inversely correlated with platelet reactivity ($p < 0.05$). Multiple logistic regression showed that 27% of the total variation in PRU was explained by a history of diabetes mellitus, hematocrit, CYP2C19*2, and PON1 p.Q192R. Body mass index (OR = 1.15; CI: 1.03–1.27), diabetes mellitus (OR = 3.46; CI: 1.05–11.43), hematocrit (OR = 0.75; CI: 0.65–0.87), and CYP2C19*2 (OR = 4.44; CI: 1.21–16.20) were the only independent predictors of HTPR. **DISCUSSION/SIGNIFICANCE OF IMPACT:** In a representative sample of Puerto Rican patients with cardiovascular disease, diabetes mellitus, hematocrit, CYP2C19*2, and PON1 p.Q192R were associated with on-treatment platelet reactivity. These factors may identify a subset of patients at higher risk for adverse events on clopidogrel in the Hispanic population.

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Day-to-day association between alcohol use and physical activity in university students

Scott Graupensperger and Michael B. Evans
Penn State Clinical and Translational Science Institute

OBJECTIVES/SPECIFIC AIMS: The goal of the present study was to advance our understanding of how alcohol use may contribute to physical inactivity among university students by investigating this association at a day-to-day level. **METHODS/STUDY POPULATION:** In total, 57 university students (Mage = 20.27; 54% male) completed daily diary questionnaires using a cellphone application, which prompted them each evening to report minutes of moderate/vigorous physical activity engaged in, and number of alcoholic drinks consumed, as well as intended minutes of physical activity for the following day. Longitudinal mixed-level modeling was used to disentangle within person and between-person effects of alcohol use on physical activity behavior and intentions. Separate models were run to investigate lagged effects of previous day alcohol use. We controlled for sex and age in all models. **RESULTS/ANTICIPATED RESULTS:** Results indicated that participants' usual alcohol use (between-person) was not associated with physical activity behavior or intentions. At the within-person level, day-to-day variance in alcohol use was negatively associated with both physical activity behavior ($\gamma = -0.34, p = 0.003$) and intentions to engage in physical activity the following day ($\gamma = -0.70, p < 0.001$). The lagged model indicated that previous day alcohol use negatively predicted PA behavior ($\gamma = -0.33, p = 0.004$).

DISCUSSION/SIGNIFICANCE OF IMPACT: Previous studies have largely been constrained to cross-sectional designs, and have surmised that there exists a positive association between alcohol use and physical activity due to trait-level differences between university students. We advance this literature by using ecological momentary assessment to investigate the within-person effects of alcohol use on physical activity at a day-to-day level while controlling for between-person variance. Contrary to existing literature, we found that on days when students consumed relatively more alcohol than they typically report, they: (a) report fewer minutes of physical activity on the same day, (b) plan to engage in relatively less physical activity on the subsequent day, and (c) engage in less physical activity on the subsequent day. By advancing our understanding of how alcohol use may curtail other health behaviors such as physical activity, we inform interventions that aim to target these behaviors in conjunction, or as part of a multiple behavior change intervention.

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Decoding/encoding somatosensation from the hand area of the human primary somatosensory (SI) cortex for a closed-loop motor/sensory brain-machine interface (BMI)

Brian Lee, Richard Andersen, Helena Chui and William Mack
University of Southern California

OBJECTIVES/SPECIFIC AIMS: A brain-machine interface (BMI) is a device implanted into the brain of a paralyzed or injured patient to control an external assistive device, such as a cursor on a computer screen, a motorized wheelchair, or a robotic limb. We hypothesize we can utilize electrical stimulation of subdural electrocorticography (ECoG) electrodes as a method of generating the percepts of somatosensation such as vibration, temperature, or proprioception. **METHODS/STUDY POPULATION:** There will be 10 subjects, who are informed, willing, and consented epilepsy patients undergoing initial surgery for placement of subdural ECoG electrodes in the brain for seizure monitoring. ECoG will be used as a platform for recording high-resolution local field potentials during real-touch behavioral tasks. In addition, ECoG will also be used to electrically stimulate the human cerebral cortex in order to map and understand how varying stimulation parameters produce percepts of sensation. **RESULTS/ANTICIPATED RESULTS:** To determine how tactile and proprioceptive signals are integrated in SI, we will perform spectral analysis of the broadband local field potentials to look for increased power in specific frequency bands in the ECoG recordings while touching or moving the hand. To explore generating artificial sensation, the subject will be asked to perform a variety of tasks with and without the aid of stimulation. We anticipate the subject's performance will be enhanced with the addition of artificial sensation. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Many patients might benefit from a BMI, such as those with stroke, amputation, spinal cord injury, or brain trauma. The current generation of BMI devices are guided by visual feedback alone. However, without somatosensory feedback, even the most basic limb movements are difficult to perform in a fluid and natural manner. The results from this project will be crucial to developing a closed loop motor/sensory BMI.

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Designing for dissemination: Characteristics of Clinical and Translational Science Award (CTSA) hubs as adopters of clinical and translational science innovation

Elaine H. Morrato¹, Lindsay Lennox² and Anne Schuster¹
¹ Colorado School of Public Health, University of Colorado, Anschutz Medical Campus, Aurora, CO, USA; ² Department of Communication, University of Colorado, Denver, CO, USA

OBJECTIVES/SPECIFIC AIMS: The Clinical and Translational Science Award (CTSA) program is a national consortium of 50+ academic medical research centers charged with accelerating the translation of clinical research. In 2017, the NIH National Center for Advancing Translational Sciences anticipates total CTSA program funding of over \$500M. The consortium's hub-and-spoke structure makes it a natural dissemination network, and the newest funding announcement makes dissemination of innovation across the consortium an explicit goal, but characteristics of CTSA hubs as adopters and transmitters of innovation are unknown. **METHODS/STUDY POPULATION:** A content analysis was conducted using data from CTSA hub Web sites ($n = 64$) and a structured coding taxonomy based on 6 constructs drawn from literature about diffusion of innovation in service organizations (Greenhalgh et al., 2004): dissemination priority, institutional complexity, communication infrastructure,

support for dissemination/implementation functions, cross-institutional collaboration/networking, and leadership composition. **RESULTS/ANTICIPATED RESULTS:** In total, 52% of hubs will renew under the new PAR in the next few years, providing an incentive to demonstrate dissemination capacity (although hubs will likely lag in operationalizing these activities until they are funded). A third of hubs (34%) represent more than one academic/research institution, and almost 80% of hubs have more than one clinical affiliate. To accommodate these different levels of institutional complexity, broad diffusion will require multi-modal, locally adapted dissemination efforts. Only 25% of hubs have capacity to undertake additional dissemination activities, and only 27% provide formal D&I support, suggesting that additional capacity/support will be needed to operationalize the CTSA dissemination mission. In total, 30% of hubs participate in cross-institutional collaboration/networking, so many may not have existing norms/tools supporting inter-institutional collaboration, but 77% include leadership from outside the School of Medicine, facilitating effective intra-institutional dissemination. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Understanding more about CTSA hubs as both adopters and transmitters of innovation can facilitate strategic use of these sites as a built-in dissemination network to amplify the reach and impact of clinical innovation and improve population health. Based on this initial analysis, the CTSA network does not appear to be fully primed for broad, rapid dissemination of innovation across its sites. In-depth interviews are being conducted to investigate CTSA hubs' perceptions of their dissemination capacity and roles as adopters and transmitters of innovation.

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Determining if intestinal commensal bacteria enhance the frequency of reassortment of an enteric, segmented virus, reovirus

Matthew Lanahan, Andrea Erickson¹ and Julie Pfeiffer¹

¹ Department of Molecular Microbiology, University of Texas Southwestern Medical Center, Dallas, TX, USA

OBJECTIVES/SPECIFIC AIMS: The overall goal is to determine if intestinal commensal bacteria play a role in enteric virus evolution. We will use reovirus, an enteric segmented virus, to investigate specific goals. First, we will determine if specific bacterial species enhance the coinfection frequency of 2 separate strains of reovirus. Second, we will determine if the presence/absence of different bacterial species in the microbiota of mice results in different reovirus reassortment frequencies. Finally, we will discover if reassortant reovirus is present in human populations. **METHODS/STUDY POPULATION:** My first goal is to determine if specific bacterial species enhance the coinfection frequency of 2 strains of reovirus. In our lab, we have a panel of commensal intestinal bacterial strains, as well as a number of lab adapted bacterial strains. We will use this panel of bacteria to determine if reovirus binds to different species of bacteria using a binding assay involving radiolabeled virus. Additionally, we will determine if specific species of bacteria alter the coinfection frequency through a Flow cytometry based assay. This will involve mixing virus with bacteria, infecting cells in culture, and straining for reovirus proteins for flow cytometry. Our second goal is to determine if specific bacteria promote reassortment of reovirus in a mouse model of infection. To do this, we will use gnotobiotic techniques to create mice harboring different intestinal bacteria populations. Mice will be infected with 2 strains of reovirus, and then feces and organs will be collected. Progeny virus will be subjected to a plaque assay on 2 different types of cells. The first type of cells will be normal cells in culture in which all viable viruses will form plaques. The second will be a cell line that stably expresses siRNAs against specific reovirus segments in which only specific reassortants will form plaques. These 2 plaque assays will be used to quantify the total number of viruses present and the total number of reassortant viruses present. Additionally, SDS-PAGE and RT-PCR will be used to confirm reassortants. Our third goal is to determine if reassortant reovirus is present in infected humans. To do this, I will obtain feces from reovirus-infected children and isolate reovirus. One specific reovirus reassortant is known to propagate in dual-infected mice. I will use the plaque assay technique to determine if this reassortant is also present in humans. To determine if other reassortants are present, I will use RT-PCR and SDS-PAGE. **RESULTS/ANTICIPATED RESULTS:** Based on previous studies with other enteric viruses, we suspect that specific bacterial species bind reovirus strains with different efficiencies. It is likely that a number of bacterial species will promote coinfection. The bacterial strains that binds both reovirus strains at a high efficiency will likely enhance coinfection by the greatest amount. It is likely that mice harboring different bacterial populations will produce different reovirus reassortment frequencies. We predict that bacteria that enhance reovirus coinfection in vitro should also enhance reovirus reassortment in our mouse model. Therefore, mice specifically lacking bacteria that promote coinfection should have significantly lower amounts of reassortant reovirus. It will be important to control for the overall amount of replication within mice with different microbiotas, as this will affect the basal reassortment frequency. We suspect

that reovirus reassortants are present in humans. Work done both in vitro and in mouse models indicates that reassortment happens at high frequencies. Additionally, one specific reassortant commonly propagates in mice due to an enhanced cellular attachment phenotype. Therefore, we predict that this reassortant also commonly emerges after coinfection and reassortment in humans. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Segmented viruses, such as influenza and rotavirus, are important human pathogens. Viral reassortment poses a unique threat to humans, as it enables new viruses to emerge and cause pandemics or epidemics. However, little is known about what factors promote viral reassortment. This study will provide insight into a novel mechanism of segmented virus evolution.

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Development and validation of a translational rat model of neonatal abstinence syndrome

Lisa Brents¹, Bryce A. Griffin¹, Caitlin Caperton¹, Lauren Russell¹, Christian Cabanlong¹, Catheryn Wilson¹, Kyle Urquhart¹, Brad Martins¹, Amy L. Patton¹, Alexander W. Alund¹, S. Michael Owens², William E. Fantegrossi² and Jeffery H. Moran¹

¹ PinPoint Testing, LLC and University of Arkansas for Medical Sciences; ² University of Arkansas Translational Research Institute

OBJECTIVES/SPECIFIC AIMS: Rodent models can be used to study neonatal abstinence syndrome (NAS), but the applicability of findings from the models to NAS in humans is not well understood. The objective of this study was to develop a rat model of norbuprenorphine-induced NAS and validate its translational value by comparing blood concentrations in the norbuprenorphine-treated pregnant rat to those previously reported in pregnant women undergoing buprenorphine treatment. **METHODS/STUDY POPULATION:** Pregnant Long-Evans rats were implanted with 14-day osmotic minipumps containing vehicle, morphine (positive control), or norbuprenorphine (0.3–3 mg/kg/d) on gestation day 9. Within 12 hours of delivery, pups were tested for spontaneous or precipitated opioid withdrawal by injecting them with saline (10 mL/kg, i.p.) or naltrexone (1 or 10 mg/kg, i.p.), respectively, and observing them for well-validated neonatal withdrawal signs. Blood was sampled via indwelling jugular catheters from a subset of norbuprenorphine-treated dams on gestation day 8, 10, 13, 17, and 20. Norbuprenorphine concentrations in whole blood samples were quantified using LC/MS/MS. **RESULTS/ANTICIPATED RESULTS:** Blood concentrations of norbuprenorphine in rats exposed to 1–3 mg/kg/d of norbuprenorphine were similar to levels previously reported in pregnant women undergoing buprenorphine treatment. Pups born to dams treated with these doses exhibited robust withdrawal signs. Blood concentrations of norbuprenorphine decreased across gestation, which is similar to previous reports in humans. **DISCUSSION/SIGNIFICANCE OF IMPACT:** These results suggest that dosing dams with 1–3 mg/kg/day norbuprenorphine produces maternal blood concentrations and withdrawal severity similar to those previously reported in humans. This provides evidence that, at these doses, this model is useful for testing hypotheses about norbuprenorphine that are applicable to NAS in humans.

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Development of human cell-based screening assays to detect subject-specific drug-response variability

Francesca Stillitano, Joshua Mayourian, Jaydev Dave, Jean-Sébastien Hulot and Roger J. Hajjar

Icahn School of Medicine at Mount Sinai

OBJECTIVES/SPECIFIC AIMS: The goals of this study are to develop a human-based screening assay for testing individual drug reactions and investigate the mechanism underlying susceptibility to develop dILQT. **METHODS/STUDY POPULATION:** We derived iPSC-CMs from 10 subjects with a high sensitivity to Sotalol (high-S group) and 10 subjects with no changes in QT interval after administration of the same drug (low-S group). Multielectrode array (MEA) was used to measure field potential duration, a surrogate to the QT interval in the electrocardiogram, in iPSC-CMs under basal conditions and in response to increasing concentrations of Sotalol. Transcriptomic profiling of iPSC-CMs from high-S Versus low-S groups was performed using RNA-sequencing. A parameter sensitivity analysis was performed on the Paci *et al.* iPSC-CM mathematical model to further support the lead hits identified via RNA-sequencing. **RESULTS/ANTICIPATED RESULTS:** Cardiac differentiation resulted in the generation of iPSC-CMs with appropriate cardiac channel