will be associated with worse clinical outcomes. (2) To examine the relationship between antipyretics and mortality in mechanically ventilated patients at risk for an acute lung injury. We hypothesize that antipyretics will have no effect on clinical outcomes in mechanically ventilated patients with and without sepsis. METHODS/STUDY POPULATION: This is a retrospective study of a "before and after" observational cohort of 1705 patients with acute initiation of mechanical ventilation in the Emergency Department from September 2009 to March 2016. Data were collected retrospectively on the first 72 hours of temperature and antipyretic medication from the EHR. Temperatures measurements were adjusted based on route of measurement. Patients intubated for cardiac arrest or brain injury were excluded from our primary analysis due to the known damage of hyperthermia in these subsets. Cox proportional hazard models and multivariable linear regression analyzed time-to-event and continuous outcomes, respectively. Predetermined patient demographics were entered into each multivariable model using backward and forward stepwise regression. Models were assessed for collinearity and residual plots were used to assure each model met assumptions. RESULTS/ANTICIPATED RESULTS: Antipyretic administration is currently undergoing analysis. Initial temperature results are reported here. In the overall group, presence of hypothermia or fever within 72 hours of intubation compared with normothermia conferred a hazard ratio (HR) of 1.95 (95% CI: 1.48–2.56) and 1.31 (95% CI: 0.97–1.78), respectively. Presence of hypothermia and fever reduced hospital free days by 3.29 (95% CI: 2.15–4.42) and 2.34 (95% CI: 1.21–3.46), respectively. In our subgroup analysis of patients with sepsis, HR for 28-day mortality 2.57 (95% CI: 1.68–3.93) for hypothermia. Fever had no effect on mortality (HR 1.11, 95% CI: 0.694–1.76). Both hypothermia and fever reduced hospital free days by 5.39 (95% CI: 4.33–7.54) and 3.98 (95% CI: 2.46–5.32) days, respectively. DISCUSSION/SIGNIFICANCE OF IMPACT: As expected, both hypothermia and fever increased 28-day mortality and decreased hospital free days. In our sepsis subgroup, hypothermia again resulted in higher mortality and fewer hospital free days, while fever did not have a survival benefit or cost, but reduced hospital free days. Antipyretic administration complicates these findings, as medication may mask fever or exert an effect on survival. Fever may also affect mechanically ventilated septic patients differently than septic patients not on mechanical ventilation. Continued analysis of this data including antipyretic administration, ventilator free days and progression to ARDS will address these questions.

2185

The effects of autoimmune inflammation on proliferation, differentiation, and androgen receptor signaling in adult prostate stem cells

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OBJECTIVES/SPECIFIC AIMS: The primary goal of this project is to verify findings from a murine prostatitis model in the human setting. METHODS/STUDY POPULATION: Methods include primary cell isolation and culture, FACS, adoptive transfer, 3D cell culture, histology, immunofluorescence, xenograft, and tissue recombination. The study population includes patients undergoing HoLEP or radical prostatectomy due to hyperplasia or adjacent bladder or prostate cancer. RESULTS/ANTICIPATED RESULTS: Having verified similar sensitivities to androgen receptor (AR) inhibitors between naive murine and human basal prostate stem cells, we anticipate that autoimmune inflammation in humans affects the response of basal prostate stem cells in a manner similar to the murine setting as well. This includes increased proliferation, increased differentiation, and decreased response to AR inhibitors. DISCUSSION/SIGNIFICANCE OF IMPACT: The identification of survival mechanisms used by basal prostate stem cells in an androgen deprived environment may give insight to the process by which prostate cancer becomes androgen independent. The effect of inflammation on proliferation, survival, and AR signaling in these cells may also provide information relevant to cancer initiation and progression.

2483

The Empower Lab: An innovative model for research experience and training for undergraduate, graduate, and medical students

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OBJECTIVES/SPECIFIC AIMS: The Empower Lab was established in 2015 with the goal of providing students with hands-on research experience in sexual and gender-based violence and health. METHODS/STUDY POPULATION: The Empower Lab consists of 10–12 undergraduate, graduate, and medical students at a time. Students undergo a rigorous application process, and agree to volunteer 8 hours per week for at least 1 year. Students are assigned to teams, and learn research skills such as literature searches, systematic reviews, research question generation, study design, IRB procedures, database creation and management, data collection and analysis, oral and poster presentation, manuscript preparation, team collaboration and communication, advocacy, and leadership. Students start as research assistants, and can be promoted to team leader, and associate director of research. Students mentor and teach each other, and are supervised by the principal investigator (PI). A survey skill self-assessment is administered to lab members on entry to the lab, every 4–6 months, and upon exit. RESULTS/ANTICIPATED RESULTS: In total, 20 students have participated in the lab to date, and 12 are currently enrolled. Eighty percent of the lab members are women. The students are 45% undergraduates, 15% graduate (nursing, social work, public health), 20% medical students, and 10% not currently enrolled in school (gap year). Twenty students completed entry surveys, 11 students have completed interim surveys, and 5 students have completed exit surveys. Examination of current surveys indicates that students are gaining skills throughout the lab experience. Free-text feedback provided further insight. Currently, the lab has 5 IRB-approved studies actively recruiting participants, 4 manuscripts being written, and 3 studies in the development phase. Students have presented at three local and 2 national meetings to date. Changes have been made to the lab structure over time in order to provide clear expectations and feedback, and strengthen student performance. DISCUSSION/SIGNIFICANCE OF IMPACT: The Empower Lab is an innovative public health lab that provides opportunities for real-world research experience for students. The teamwork, collaboration, and structure of the lab permit mentoring, support, and teaching from peers, as well as from the PI. The Lab increases the PI's productivity. Students are encouraged to develop and implement their own research ideas, further encouraging independence and initiative. Although the number of surveys is limited to date, they indicate improvement in skills and confidence among lab members. The predominance of women in the lab suggests that this is a strong model for recruitment and retention of women in STEM.

2406

The microbial-derived short-chain fatty acid butyrate directly and differentially inhibits gut T helper cell subset activation and proliferation

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OBJECTIVES/SPECIFIC AIMS: A hallmark of progressive HIV-1 infection is the massive activation and depletion of the gut barrier protective CD4 T helper subsets (Th17 and Th22) in the intestinal mucosa. The loss of these cells is thought to contribute to microbial translocation and systemic immune activation that occurs during chronic infection. In addition to the loss of protective Th subsets, we previously showed that chronically HIV-1 infected individuals have an altered colonic mucosal microbiome, which is in part characterized by a lower relative abundance of bacteria that produce the short-chain fatty acid butyrate in conjunction with increased relative abundance of gram-negative pathobionts. This dysbiosis was linked to markers of mucosal and systemic immune activation in these individuals. Following up on these clinical observations, we sought to understand how a loss of butyrate might contribute to HIV-associated inflammation. Initial studies showed that the addition of butyrate to cultured lamina propria mononuclear cells (LPMC) resulted in decreased pathobiont-driven gut T cell activation, HIV-1 infection levels and production of IL-17 and IFNy. Since the gut barrier protective Th17 and Th22 subsets are preferentially infected and depleted, which is critical to HIV-1 pathogenesis, we wanted to determine the mechanism by which butyrate modulates activation of these important Th subsets in the gut. METHODS/STUDY POPULATION: Total LPMCs or purified LP CD4 T cells were isolated from human jejunal tissue (n = 3–6), labeled with CFSE and cultured with TCR/CD28 beads to mimic APC driven T cell activation, with the addition of butyrate at physiologic doses(0–2 mM). Four days after culture, secreted cytokine(IL-17 and IFNy) levels were measured by ELISA. Cells were then short-term (4 hr) mitogenically stimulated (PMA/Ionomycin) in the presence of a golgi transport inhibitor. Total CD4 T cell activation (CD38 + /HLA-DR + , CD25 +), proliferation (CFSElow), and frequencies of intracellular cytokines were measured by multi-color flow cytometry. Paired *t*-tests were performed to determine statistical significance. RESULTS/ANTICIPATED RESULTS: Butyrate inhibited LP CD4 T cell activation ($p = 0.013$) and proliferation ($p = 0.015$) within total LPMCs stimulated with TCR/CD28 beads in a dose-dependent manner, with significant activity starting at 0.125 mM. Quantification of total secreted cytokines revealed that butyrate significantly decreased both IL-17 and

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IFNy production after 4 days of culture at 0.0625 mM and 0.25 mM of butyrate, respectively. Assays using purified LP CD4 T cells demonstrated that butyrate directly decreased LP CD4 T cell activation, proliferation and cytokine production in response to TCR/CD28 stimulation. Studies on specific T helper subsets revealed that butyrate inhibited proliferation of Th17 cells at lower concentrations (IC50:0.147 mM) compared with Th1 (IC50:0.229 mM) and Th22 (IC50:0.258 mM) and Th non-IL-22/IL-17/IFNy producing (IC50:2.14 mM) subsets. In addition, it appeared there was a paradoxical increase of HIV-1 infection levels at lower concentrations of butyrate (0.125 mM). DISCUSSION/SIGNIFICANCE OF IMPACT: The addition of butyrate to activated LP CD4 T cells decreases TCR-mediated activation in a dose-dependent manner, and butyrate acts directly on purified LP CD4 T cell populations independent of other cell populations. Butyrate differentially inhibited the proliferation of Th17, Th1, and Th22 subsets, with Th17 cells being the most sensitive to butyrate but increased the infection levels of all T helper subsets at low concentrations. Further studies are needed to determine the mechanism of butyrate's actions on LP Th cells and the sensitivity of Th17 cells to the inhibitory effects of butyrate. These results could help direct targeted manipulation of the colonic microbiome of HIV-1 infected individuals to help resolve inflammation and limit the impact of the infection in the gut mucosa and systemically.

2349

The role of interleukin-23 in human melanoma

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OBJECTIVES/SPECIFIC AIMS: Interleukin-23 (IL-23) promotes differentiation of naïve T-cells into Th17 cells, which drive the pathogenesis of autoinflammatory conditions such as psoriasis. IL-23-neutralizing antibody therapies are now in use for treatment of psoriasis, with promising results. Studies in mice have shown that IL-23 plays a role in inhibiting the growth, progression, and metastasis of melanomas. Thus, therapeutic neutralization of IL-23 in patients may inadvertently increase their susceptibility to development of melanoma. In this study, we aim to characterize expression of IL-23 receptors (IL-23R) in human melanocytes and melanoma cells and tissue and to study the effect of IL-23 on growth, proliferation, and tumorigenicity of these cells. METHODS/STUDY POPULATION: IL-23R expression was characterized using immunofluorescence staining, Western blot, and flow cytometric analysis. Response of melanoma and melanocytes to recombinant IL-23 treatment will be studied through similar methods in addition to assays of cell proliferation and tumorigenicity. RESULTS/ANTICIPATED RESULTS: Preliminary immunofluorescence staining and flow cytometry results indicate that both human melanoma and primary melanocytes express IL-23 receptors. Western blot analysis showed that melanoma cell line A375 expressed nearly twice the amount of IL-23R versus normal melanocytes ($p < 0.05$). Based on previous studies, we anticipate that addition of recombinant IL-23 to cultures of melanoma will reduce proliferative potential, and we expect similar addition to normal melanocytes will increase DNA repair mechanisms. DISCUSSION/SIGNIFICANCE OF IMPACT: In showing that human melanocytes and melanoma cells express IL-23 receptors, and potentially showing the inhibitory effect of IL-23 in the development of melanocytic neoplasms, our findings imply that using IL-23 neutralizing therapies may increase risk of developing melanoma, especially in patients who are already susceptible. As such, these therapies must be used with great care in these patients.

2153

The plasma contact system and its role in common variable immunodeficiency (CVID): An explorative study

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OBJECTIVES/SPECIFIC AIMS: Assess the presence of contact activation at baseline in sera from common variable immunodeficiency (CVID) patients with and without inflammatory complications compared with healthy controls. METHODS/STUDY POPULATION: CVID patients were recruited in the outpatient setting and the measurement of cleaved plasma HK (cHK) levels was determined by Western blot analysis, under reducing conditions, with quantitation of total and cHK bands using an Odyssey imaging system (Licor). One-way ANOVA test for differences among the 3 studied groups will be applied. Biomarkers C3, C4, C1 inhibitor levels and hs-CRP were also measured. RESULTS/ANTICIPATED RESULTS: Participant enrollment continues and to date, 9 CVID patients were studied, 7 with and 2 without inflammatory complications. Repeated determinations of cleaved HK% (cHK%) revealed an average of 1.20% (range: 0.46%–2.66%) in CVID patients with inflammatory complications and those without complications averaged 1.07% (range: 0.79%–1.35%). Healthy controls had an average cHK of 1.15% (range: 0.60%–2.10%). DISCUSSION/SIGNIFICANCE OF IMPACT: Cleaved kininogen detected in the sera of CVID patients was found at similar levels compared with healthy controls (cHK < 5%). Findings suggest that systemic activation of the contact system might be absent in CVID, however, future considerations include developing detection methods for local tissue activation.

2356

The nasopharyngeal microbiome is perturbed and associated with increased clinical severity during acute respiratory viral infection

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OBJECTIVES/SPECIFIC AIMS: We sought to investigate the role of the host microbiome during severe, acute respiratory infection (ARI) to understand the drivers of both acute clinical pathogenesis. METHODS/STUDY POPULATION: Nasopharyngeal swabs comprised of mixed cell populations at the active site of infection were collected from 192 hospitalized pediatric patients with ARI. We combined comprehensive respiratory virus detection and virus genome sequencing with 16S rRNA gene sequencing to evaluate the microbial content of the airway during ARI. This data was coupled with 11 clinical parameters, which were compiled to create a clinical severity score. The microbiome profiles were assessed to determine if clinical severity of infection, and/or specific virus was associated with increased clinical severity. RESULTS/ANTICIPATED RESULTS: We identified 8 major microbiome profiles classified by dominant bacterial genus, Moraxella, Corynebacterium, Staphylococcus, Haemophilus, Streptococcus, Alloiococcus, Schlegelella, and Diverse. Increased clinical severity was significantly associated with microbiome profiles dominated by Haemophilus, Streptococcus, and Schlegelella, whereas Corynebacterium and Alloiococcus were more prevalent in children with less severe disease. Independent of the microbial community, more than 60% of patients with the highest clinical severity were infected with either respiratory syncytial virus or rhinovirus. DISCUSSION/SIGNIFICANCE OF IMPACT: Our results indicate that individually and in combination, both virus and microbial composition may drive clinical severity during acute respiratory viral infections. It is still unclear how the complex interplay between virus, bacterial community, and the host response influence long-term respiratory impacts, such as the development of asthma. Nonetheless, during ARIs therapeutic interventions such as antibiotics and probiotics may be warranted in a subset of patients that are identified to have both a virus and microbiome profile that is associated with increased pathogenesis to limit both acute and long-term phenotypes.

2027

The role of lysyl oxidase in systemic sclerosis-associated lung fibrosis

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OBJECTIVES/SPECIFIC AIMS: Systemic sclerosis (SSc) is a connective tissue disease of unknown etiology characterized by progressive fibrosis of the skin and multiple visceral organs. Effective therapies for SSc are needed. Lysyl oxidase (LOX) is a copper-dependent amide oxidase that plays a critical role in the crosslinking of the extracellular matrix (ECM). In this study, we investigated the role of LOX in the pathophysiology of SSc. METHODS/STUDY POPULATION: LOX expression and protein levels were measured in lung tissues and primary fibroblasts from patients with SSc and healthy controls. The effects of recombinant LOX (rLOX) were measured in vitro in primary fibroblasts, ex vivo in human lung tissues and in vivo in mice given bleomycin in combination with rLOX. LOX levels and activity were evaluated in lung fibroblasts treated with an endostatin-derived peptide that ameliorates fibrosis

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