

High dose group ($n=6$) received $2W/cm^2$ for 2 minute with 0.7 mL microbubbles IV. Perfusion was measured before and after AVUS with contrast-enhanced ultrasound (CE-US) and power Doppler (PD-US). Peak enhancement (PE) and perfusion index (PI) were measured from each US mode. Histology after sacrifice or natural death was compared to pre/post US. Analysis of H&E and trichrome sections was evaluated for percent area of hemorrhage and findings of tissue injury and repair including inflammation, necrosis, and fibrosis. RESULTS/ANTICIPATED RESULTS: After high dose AVUS, PE, and PI of CE-US decreased from baseline by an average of 33.3% and 29.7%, respectively. Histology showed extensive tissue injury (hemorrhage, necrosis, fibrosis) in 58% of tumor cross-sectional area. Conversely, low dose AVUS increased PE and PI of CE-US by an average of 39.3% and 67.8%, respectively. Histology showed smaller areas of microhemorrhage versus large pools of hemorrhage (only 17% area). PD-US changes were similar to CE-US. DISCUSSION/SIGNIFICANCE OF IMPACT: In summary, the opposing effects of AVUS observed at 2 doses allows for multiple roles in tumor therapy. Enhanced perfusion at a low dose may improve drug delivery or radiation therapy. Whereas, vascular disruption at high doses of AVUS may allow noninvasive ischemic therapy. Furthermore, AVUS is ripe for translation given the use its component parts clinically: low-intensity long-tone burst for physiotherapy and microbubbles as an US contrast agent. Thus, AVUS should be evaluated for translation of its differential effects into noninvasive therapies for HCC and other tumors.

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Cardiac injury due to *Streptococcus pneumoniae* invasion during severe pneumococcal pneumonia in a novel nonhuman primate model

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OBJECTIVES/SPECIFIC AIMS: The aims of this study are (1) to develop and characterize a novel nonhuman primate model of pneumococcal pneumonia that mimics human disease; and (2) determine whether *Streptococcus pneumoniae* can: (a) translocate to the heart, (b) cause adverse cardiac events, (c) induce cardiomyocyte death, and (d) lead to scar formation during severe pneumonia in baboons. METHODS/STUDY POPULATION: Six adult baboons (*Papio cynocephalus*) were surgically tethered to a monitoring system to continuously assess their heart rate, temperature, and electrocardiogram (ECG). A baseline transthoracic echocardiogram, 12-lead ECG, serum troponin-I levels, brain natriuretic peptide, and heart-type fatty acid binding protein (HFABP) levels were obtained before infection and at the end of the experiment to determine cardiovascular damage during pneumococcal pneumonia. Animals were challenged with 108 colony-forming units of *S. pneumoniae* in the right middle lobe using flexible bronchoscopy. Three baboons were rescued with ampicillin therapy (80 mg/kg/d) after the development of pneumonia. Cardiac damage was confirmed by examination of tissue sections using immunohistochemistry as well as electron and fluorescence microscopy. Western-blot and tissue staining were used to determine the presence of necroptosis (RIP3 and pMLKL) and apoptosis (Caspase-3) in the cardiac tissue. Cytokine and chemokine levels in the heart tissue were determined using Luminex technology. RESULTS/ANTICIPATED RESULTS: Four males (57%) and three (43%) females were challenged. The median age of all baboons was 11 (IQR, 10-19) years old, which corresponds to a middle-aged human. Infected baboons consistently developed severe pneumonia. All animals developed systemic inflammatory response syndrome with tachycardia, tachypnea, fever, and leukocytosis. Infection was characterized by initial leukocytosis followed by severe leukopenia on day 3 postinoculation. Non-specific ischemic alterations by ECG (ST segment and T-wave fluttering) and in the pre-mortem echocardiogram were observed. The median (IQR) levels of troponin I and HFABP at the end of the experiment were 3550 ng/mL (1717–5383) and 916.9 ng/mL (520.8–1323), respectively. Severe cardiomyopathy was observed using TEM and H&E stains in animals with severe pneumonia. Necroptosis was detected in cardiomyocytes of infected animals by the presence of pMLKL and RIP3 in cardiac tissues. Signs of cardiac remodeling indicated by disorganized collagen deposition was present in rescued animals but not in the

other animals. DISCUSSION/SIGNIFICANCE OF IMPACT: We confirmed that baboons experience cardiac injury during severe pneumococcal pneumonia that is characterized by myocardial invasion, activation of necroptosis, and tissue remodeling in animals rescued by antimicrobial therapy. Cardiac damage by invading pneumococci may explain why adverse cardiac events that occur during and after pneumococcal pneumonia in adult human patients.

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Central autonomic network dysfunction implicated in alcohol-related intimate partner violence

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OBJECTIVES/SPECIFIC AIMS: Most incidents of partner violence occur when one or both partners have been drinking, however, the mechanism through which this association exists is unclear. The neural circuits that support self-regulation of emotion and social behavior, as well as autonomic influences on the heart, are co-localized in the brain and represent an integrated bidirectional regulatory system. These physiological regulatory processes are mediated by a neural substrate known as the central autonomic network which includes the peripheral autonomic nervous system. The central autonomic network modulates biobehavioral resources in emotion by flexibly responding to physiological arousal in response to changing situational demands, and serves a fundamental role in emotion regulation and goal-directed motor behavior, and this circuit can be indexed with heart rate variability (HRV). METHODS/STUDY POPULATION: In total, 17 distressed violent (DV) partners (11 females, 6 males) were matched to a sample of distressed nonviolent (DNV) partners (7 female, 6 males) were matched on age, sex, and relationship satisfaction and participated in a placebo-controlled alcohol administration study with an emotion-regulation task during which electroencephalography, HRV, and galvanic skin response (GSR) measures were collected. In the alcohol condition, participants were administered a mixture of 100 proof vodka and cranberry juice calculated to raise their blood alcohol concentration to 0.08%. In the placebo condition, participants consumed a volume of juice equivalent to that consumed in the alcohol condition, but without alcohol. Alcohol and placebo conditions were counter-balanced across participants as were the presentation of the blocks of evocative and neutral partner stimuli and emotion-regulation condition (watch vs. do not react). RESULTS/ANTICIPATED RESULTS: Results show that DV partners show greater cortical arousal than DNV partners on measures event-related spectral perturbations, which are mean log event-locked deviations from baseline-mean power at each frequency of the electroencephalography power spectra, when intoxicated and viewing evocative partner stimuli in the “do not react” emotion regulation condition. Results also show a statistically significant 2 (alcohol vs. placebo) \times 2 (watch vs. do not react) \times 2 (DV partners vs. DNV partners) interaction of the respiratory sinus arrhythmia measure of HRV when viewing evocative partner behavior ($F=7.102$, $p=0.019$, partial $\eta^2=0.353$). Findings indicate that DV partners have lower HRV than DNV partners across conditions, but particularly when acutely intoxicated and trying not to react to their partners’ evocative behavior. Similarly, results also show a statistically significantly 2 (alcohol vs. placebo) \times 2 (watch vs. do not react) \times 2 (DV partners vs. DNV partners) interaction on GSR ($F=71.452$, $p=0.000$, partial $\eta^2=0.749$). GSR findings indicate that DV partners also have lower GSR when acutely intoxicated and trying not to react to their partners’ evocative behavior. DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that increases in intimate partner violence under acute alcohol intoxication may be the result of dysfunction of the central autonomic network, especially when DV partners are trying to suppress a behavioral response to their partners’ evocative behavior in conflict. The neurophysiological patterns evidenced by DV partners is consistent with a state of vigilance to threat, and reduced ability inhibit prepotent, but inappropriate responses. They also suggest that HRV may be an important target for intervention with partner with a history of intimate partner violence. One method may be heart rate variability biofeedback which has been shown to increase parasympathetic nervous system functioning, autonomic stability, and emotion regulation.

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Characterizing specialized pro-resolving lipid mediators and synthesis pathways in veterans with peripheral artery disease

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OBJECTIVES/SPECIFIC AIMS: Specialized pro-resolving lipid mediators (SPM) actively counter proinflammatory cascades. A deficit of SPMs is one possible mechanism through which inflammation leads to the development of atherosclerotic disease. The purpose of this study is to characterize the profiles

of intermediates of SPM synthesis pathways and end-product SPMs in the plasma of patients with peripheral artery disease (PAD). **METHODS/STUDY POPULATION:** A cross-sectional sample of 52 patients with PAD was recruited at the San Francisco Veterans Affairs Medical Center. PAD was defined as the presence of claudication symptoms and an ankle-brachial index <0.9, or a history of revascularization for claudication. Patients were excluded if they were taking immunosuppressive medications, had a severe acute illness (infection, surgery, illness, critical limb ischemia) within the last 30 days, or had severe hepatic, renal, or nonvascular inflammatory disease. Intermediates of SPM synthesis pathways and end-product SPMs were measured in plasma samples of patients by liquid chromatography-tandem mass spectrometry. **RESULTS/ANTICIPATED RESULTS:** The average age of the cohort was 69 ± 6.3 and patient comorbidities reflected common comorbidities associated with PAD (hypertension 96%, hyperlipidemia 87%, diabetes mellitus 42%, coronary artery disease 34%). Rutherford categories, measurements of PAD symptom severity, ranged from 0 to III (0 10%, I 40%, II 27%, III 23%). Three EPA products were measured: 18-hydroxyeicosapentaenoic acid (18-HEPE), resolvin E1 (RvE1), and resolvin E2 (RvE2). 18-HEPE, an intermediate of SPM synthesis, was detectable in the plasma of every patient (median: 105 pg/mL, IQR: 54.9–195), whereas the SPM end-products, RvE1 and RvE2, were only detectable in 6 and 10 patients, respectively. In total, 7 DHA products were measured: 14-hydroxydocosahexaenoic acid (14-HDHA), 17-HDHA, resolvin D1 (RvD1), resolvin D2 (RvD2), protectin D1, protectin DX, and maresin 1. The intermediates 14-HDHA (median: 6546 pg/mL, IQR: 3329–12061) and 17-HDHA (median: 644 pg/mL, IQR: 340–1056) were detectable in the plasma of every patient. However, the end-products RvD1, RvD2, protectin D1, protectin DX, and maresin 1 were identified in less than half of the cohort. **DISCUSSION/SIGNIFICANCE OF IMPACT:** We report the presence of several intermediates of SPM synthesis pathways (18-HEPE, 14-HDHA, and 17-HDHA) in every patient but the presence of SPM end-products in only a limited portion of the cohort. These results suggest that some patients with PAD may have a deficit of SPMs. Further investigation is required to better understand the role of SPMs and mediators of resolution of inflammation in PAD.

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Characterizing the expression kinetics of HIV-1 envelope protein

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OBJECTIVES/SPECIFIC AIMS: Characterize the expression kinetics of HIV-1 Envelope and their relationship to virus production at the cellular level. **METHODS/STUDY POPULATION:** In vitro and ex vivo laboratory analyses. **RESULTS/ANTICIPATED RESULTS:** Initial studies addressing the kinetics of cell surface. Envelope (Env) expression reveal that Env expression peaks on day 2 post infection. Next steps include a series of experiments to compare the kinetics of Env cell surface expression with broadly neutralizing antibody (bNAb)-mediated ADCC and the characterization of virus production kinetics in this same context. To be maximally effective, ADCC elimination of infected cells should occur before peak Env expression. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Potent bNAbs to HIV-1 recognize vulnerable sites on the HIV-1 Envelope (Env) protein and are of great clinical interest due to their potential use in the prevention and treatment of HIV-1 infection. Their effectiveness depends not only on the neutralization of viral infectivity, but also on the elimination of productively infected cells via antibody-dependent cellular cytotoxicity (ADCC). On a cellular level, ADCC dynamics are determined by the timing and level of Env expression on the surface of HIV-1 infected cells. This study aims to delineate the expression kinetics of HIV-1 Envelope and their relationship to virus production. We expect that it will provide new insights into the utility of bNAb-mediated ADCC in treating and possibly curing HIV-1 infection; therefore results might have substantial impact on future HIV treatment strategies.

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Community forums as a channel for communicating with the public and to influence perceptions of cancer clinical trials

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OBJECTIVES/SPECIFIC AIMS: Cancer clinical trials (CCTs) are vital tools in the advancement of cancer prevention and treatment. Yet, only 3%–5% of eligible

patients enroll in CCTs. Low participation can be attributed, in part, to poor communication as well as a lack of awareness and understanding about CCTs. In order to increase participation in trials, interventions should foster meaningful communication about cancer prevention and CCTs, especially between medical professionals and members of the community. Community forums provide a channel to communicate about cancer with members public and to educate prospective participants about CCTs. Thus, our goal was to evaluate the efficacy of hosting community forums about cancer in order to educate the public and influence perceptions of CCT participation. **METHODS/STUDY POPULATION:** During the Spring of 2016, participants (n = 51) who attended a community forum about CCTs completed a pretest and post-test survey assessing their understanding and perceptions of CCTs. **RESULTS/ANTICIPATED RESULTS:** Results from the pretest to post-test survey revealed a significant positive increase ($p = 0.01$) in participants' attitudes toward cancer clinical research as well as marginally significant increases in participants' perceived subjective norms ($p = 0.06$) about participating in CCTs and the perceived personal relevance ($p = 0.06$) of clinical research participation pretest and post-test. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Findings suggest that community forums about cancer and CCTs could lead to an increased awareness and understanding of CCTs among members of the population and could be useful channels for cancer interventions.

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Creating a comprehensive municipal inventory of common ragweed (*Ambrosia artemisiifolia*) to predict allergenic pollen exposures

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OBJECTIVES/SPECIFIC AIMS: One of the key difficulties in predicting allergenic pollen exposures has been a lack of information on source plant location and abundance. However, the increasing availability of spatially explicit data from remote sensing offers new opportunities to create comprehensive inventories of allergenic pollen producing plants. **METHODS/STUDY POPULATION:** In this study, we use a spatially oriented field survey to map common ragweed (*Ambrosia artemisiifolia*) in Detroit, MI, USA. We then combine this with remote sensing imagery and LiDAR to predict ragweed presence and potential pollen production across 344 km² of Detroit. Finally, we compare this with measurements of airborne pollen concentrations collected throughout the city. **RESULTS/ANTICIPATED RESULTS:** Our initial results show that ragweed is present in ~2% of the city, and its presence and abundance are strongly associated with demolished building ($p < 0.001$). The uneven distribution of ragweed plants across the city leads to substantially higher pollen concentrations in neighborhoods where more buildings have been recently demolished. **DISCUSSION/SIGNIFICANCE OF IMPACT:** Our approach offers an effective way to quantify allergenic pollen production, airborne concentrations, and exposures across a large metropolitan area. This in turn provides insight on how to best reduce airborne pollen concentrations: in this case, by changing post-demolition land management practices.

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Cutaneous lupus erythematosus patients have increased circulating myeloid-derived suppressor cells with immunosuppressive properties

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OBJECTIVES/SPECIFIC AIMS: MDSCs are potent suppressors of T cell function, and have been recently found to be implicated in skin diseases driven by T cell dysregulation. However, the function of MDSCs in CLE is poorly understood. We sought to characterize the MDSC population in the peripheral blood of DLE patients and evaluate their ability to suppress autologous T cells. **METHODS/STUDY POPULATION:** All patients were recruited through the UT Southwestern Cutaneous Lupus Registry. PBMCs from 32 CLE patients and 16 age-matched and gender-matched controls were analyzed using flow cytometry. Monocytic MDSCs were identified by the phenotype of CD14⁺ HLA-DR^{neg/low}. Furthermore, autologous MDSCs and T cells were purified from CLE PBMCs (n = 4) and cocultured at different ratios of these cells. T cell function was measured by secretion of IFN- γ by ELISA. **RESULTS/ANTICIPATED RESULTS:** Monocytic MDSCs in CLE PBMCs (median: 2.04%, IQR: 0.67%–5.07%) were significantly higher compared with healthy control PBMCs (median: 0.5%, IQR: 0.1%–1.07%, $p = 0.002$). Although not significant on subset analysis, patients with CLE limited to the head and neck had the highest levels of MDSCs. CLE MDSCs (n = 4) were found to suppress