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OBJECTIVES/GOALS: We endeavor to investigated the hypothesis that muscle protein synthesis (MPS) is stimulated more after consumption of a 4-ounce beef patty as compared to 4- and 8-ounces of a soy protein based meat alternative (SPBMA) and if a greater stimulation is related to differences in the responses of plasma essential amino acid (EAA) concentrations. METHODS/STUDY POPULATION: Participants were aged 18 to 40 years of age with a BMI between 20 and 32 kg/m2. Written informed consent was obtained from all participants, and approved by UAMS IRB. Participants were assigned to one of three intervention groups via a single-blinded permuted block randomization, stratified for sex: 4 oz beef patty; 4 oz SPBMA; 2 x 4 oz (8oz) SPBMA. The impossible burgerTM was selected as it is primarily soy protein, a high-quality plant protein, and specifically designed to mimic a beef burger. Stable isotope were infused to assess protein metabolism. Appropriate muscle and blood samples were obtained. Enrichment and plasma EAA concentrations were measured with mass spectrometry. ANOVA's on the change from basal to postprandial were used to identify group difference, significance was accepted at $p < 0.05$. RESULTS/ANTICIPATED RESULTS: The MPS increase from basal to postprandial indicated a significant main effect of group ($p = 0.026$), with the beef group (0.020 ± 0.016%/hour) being significantly greater than the 4oz SPBMA (0.003 ± 0.010%/hour; $p = 0.021$) but not the 8oz PBMA group (0.013 ± 0.016%/hour; $p = 0.454$). Similar results were observed for whole-body protein synthesis, where the beef group ($p = 0.042$) and 8oz SPBMA ($p = 0.033$) were significantly greater than the 4oz SPBMA ($p = 0.021$). Whole-body protein balance was significantly greater in the 8oz SPBMA as compared to 4oz of beef and SPBMA. Lastly, we observed a significantly relationship ($p = 0.046$; $r = 0.411$) between the maximal plasma EAA concentration and change in MPS, indicating the greater rate of MPS following 4oz of beef is mediated by an higher increase in plasma EAA concentrations. DISCUSSION/SIGNIFICANCE: In conclusion, 4oz of beef stimulates muscle protein FSR more than 4oz of a SPBMA. A common SPBMA can stimulate increase in protein metabolism, however, greater amounts are required as compared to beef protein. Further, the change in the muscle protein FSR response was significantly correlated with the maximal EAA concentration.

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Transcriptomic analysis of Influenza A infected lung organoids reveals Warburg-like phenotype*

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OBJECTIVES/GOALS: The CDC estimates that Influenza infections account for an average of 420,000 hospitalizations and 34,700 deaths in the U.S. each year. This project explores the underlying mechanisms of the infectious process of Influenza A in human lung organoids by examining the differential transcriptomic expression compared to uninfected controls. METHODS/STUDY POPULATION: Lung organoids were cultured from differentiated human bronchial epithelial cells from lung transplant donors on an air-liquid interface until they were confirmed to contain both mucous producing and ciliated cells. Lung organoids are ideal models in translational science due to their structural and functional characteristics which closely mimic those of in vivo human epithelial tissue. Half the organoids were exposed to Influenza A pH1N1 for 72h; the other half served as uninfected controls. RNA was isolated from both groups and sequenced using the Oxford Nanopore MinION which generates full length reads. Reads were aligned to the human reference genome (GRCh38.p14) using Minimap2. RESULTS/ANTICIPATED RESULTS: The MinION sequenced an average of 3.24m reads per sample and a total of 13,128 genes were relevantly expressed (defined as greater than 1 read per million in at least half the samples). ANOVA with a 5% false discovery rate (Benjamini and Hochberg correction) revealed 5,417 differentially expressed genes between infected and control groups. Within this subset, we identified downregulation of mucociliary clearance, mitochondrial and ÃŸ-oxidation, peroxisome, and glutathione replenishment genes. We further identified upregulation in inflammatory markers, lactate dehydrogenase enzymes, and several s100 proteins. The downregulation of mitochondrial and β-oxidation markers and the upregulation of lactate dehydrogenase enzymes revealed a Warburg-like phenotype which has not previously been reported. DISCUSSION/SIGNIFICANCE: This study reveals a novel Warburg-like phenotype in Influenza A infection alongside downregulated mucociliary clearance and upregulated inflammatory processes. These findings improve our understanding of Influenza A infection and point to potential therapeutic targets to advance precision medicine approaches to treatment.

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Treatment experience and symptom burden in multiple myeloma: interim results of a longitudinal electronic patient-reported outcomes study

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OBJECTIVES/GOALS: Patients with multiple myeloma (MM) experience significant disease- and treatment-related symptom burden, especially with higher lines of therapy (LOT). We used a remote symptom monitoring app to characterize overall symptom profile, symptom bother, and quality of life (QOL) among patients with MM across LOT and longitudinally. METHODS/STUDY POPULATION: We used Carevive PROmpt, a symptom monitoring app for cancer patients. From 11/10/22 to 9/27/23, we enrolled 84 adult patients with MM of any stage and anywhere in the treatment continuum from Duke Health MM clinics. Participants received weekly symptom surveys while on active treatment. Per prior studies, we defined heavily pretreated patients as those on current LOT ≥4. Our sample had a mean (SD) age of 63.7 (10.8) years and was 56.0% male; 73.8% had a prior bone marrow transplant, 40.5% were on LOT ≥4 (53.6% on LOT <4, 6.0% missing), 58.3% were on triplet therapy or higher. For 14 symptoms, we described the prevalence of moderate to very severe (MOD-VS) symptoms based on LOT overall and over time. We also described responses to "How bothersome are treatment side effects?" and "Overall QOL over the past week" based on LOT. RESULTS/ANTICIPATED RESULTS: Surveys continued for a mean (SD) of 14.9 (9.6) weeks (range: 44). The top 5 MOD-VS symptoms ever experienced were fatigue

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(66.7% of patients), neuropathy (48.8%), muscle pain (44.0%), insomnia (39.3%), and general pain (38.1%). Patients on LOT ≥4 had most of these symptoms more often than LOT <4 (fatigue: 70.6% of patients vs. 60.0%, neuropathy: 71.8% vs. 40.0%, muscle pain: 47.1% vs. 42.2%, insomnia: 35.3% vs. 40.0%, general pain: 47.1% vs. 33.3%). For those on LOT ≥4, 42.9% of survey responses endorsed "somewhat", "quite a bit", or "very much" symptom bother compared to 32.7% for LOT <4. QOL was similar between groups. Over many months, patients on LOT ≥4 had several persistent symptoms (neuropathy, sadness, insomnia), but even those on LOT <4 had unmet symptom needs (fatigue, general pain, constipation). DISCUSSION/SIGNIFICANCE: Evidence shows that treatment selection at higher LOT in MM often underrates the impact of cumulative symptom burden. Our study reveals significant longitudinal unmet needs regarding symptom and distress management in MM; understanding this can help guide treatment decisions and palliative care for MM patients with escalating treatment demands.

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Deciphering the role of IL-4 in post-colitis repair*

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OBJECTIVES/GOALS: Incomplete mucosal healingand dysbiosis prevent long-term remission after colitis. IL4 may restore colon homeostasis through its action on immune cells and the microbiome. We will demonstrate this mechanism using genetically modified mice and molecular tools. This may result in target therapies that prolong remission in patients with IBD. METHODS/STUDY POPULATION: Mice were treated with 3% dextran sulfate sodium (DSS) in drinking water for 5 days to induce colitis. Mice were monitored daily for changes in body weight, and to monitor colitis severity. At each endpoint, mice were sacrificed and colon length was measured. For disease severity assessment, mouse colons were prepared in paraffin sections by the 'swiss-rolling' method. For flow cytometry, lamina propria mononuclear cell isolation was performed and cellular populations were stained with fluorophore-conjugated antibodies. IL4-eGFP-expressing (4get) mice were used to analyze the cellular expression of IL4 after colitis. Cell-specific IL4 deletion mice were generated using the cre-lox system. RESULTS/ANTICIPATED RESULTS: IL4-deficient mice had worse colitis compared with wild-type controls. Flow cytometry of lamina propria cells from 4get mice showed that most IL4-producing cells after colitis are eosinophils (CD11b+SiglecF+). Flow cytometry of C57bl6 mice showed an influx of IL4Ra+ monocytes (CD11b+Ly6C+) and macrophages (CD11b+F480+). IL4-stimulated bone marrow-derived macrophages demonstrated an increase in HB-EGF mRNA transcription. Myeloid-specific IL4R deleted mice had no difference in colitis severity compared with controls. Neutrophil-specific IL4R-deleted mice had increased colitis severity and mortality. Co-housing of littermate mice rescued recovery after DSS in IL4 deficient mice. DISCUSSION/SIGNIFICANCE: IL4 appears to play a role in restoring homeostasis after colitis. The mechanism depends on eosinophil-derived IL4, and action through neutrophils. However, the reparative function of IL4 can be shared with deficient mice through the microbiome. I will study the cellular and microbial mechanism by which IL4 restores homeostasis after colitis.

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Identifying neural and behavioral correlates of social learning and empathetic responding associated with early life adversity

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OBJECTIVES/GOALS: This study seeks to elucidate the relationships between early life adversity (ELA), social learning, and empathic responding. Specifically, it aims to understand the impact of ELA on the expression of empathy and ability to adjust behavior after social observation. METHODS/STUDY POPULATION: 60 healthy participants ages 18-65 will be recruited from the greater Baltimore area. They will undergo a placebo manipulation paradigm with simultaneous EEG recording to capture neural oscillations in frontal and insular cortices and event-related potentials. Participants will observe a demonstrator who indicates pain relief in response to the application of an inert cream. Then, while undergoing heat pain stimulations, the participant will receive the same inert cream and rate their physiological and psychological pain experience using a visual analog scale. The heat stimulations will be lowered without their knowledge to measure placebo response. Participants will also answer a battery of questionnaires which assess personality, psychological factors, life history, empathy, and current social life. RESULTS/ANTICIPATED RESULTS: It is expected that ELA will result in decreased placebo response, interpreted as deficits in social learning. Further, we expect that this effect is moderated by state empathy, empathy in a specific context or moment. We predict that individuals with lower state empathy and exposure to adversity will have greater deficits in social learning. We also expect to see more robust event-related potentials preceding painful stimulations at electrodes corresponding to the medial and ventral prefrontal cortex and insula in ELA-exposed participants. Because these brain regions are connected to anticipatory and predictive circuits, this would indicate that the individual has not adjusted their expectations according to the social information gained via observation. DISCUSSION/SIGNIFICANCE: Results of this study will expand our understanding of how ELA impacts behavior throughout life. Individuals with a history of ELA often face social difficulties and a higher risk of psychiatric disorders. This study will illuminate possible neural correlates of these differences in social behavior and, more generally, the expression of empathy.

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Deformable Medial Modeling to Generate Novel Shape Features of the Placenta Using Automated versus Manual Segmentations*

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OBJECTIVES/GOALS: In this study, we implemented deformable medial modeling as a morphometric approach in first trimester placentas to characterize morphometric differences between fully

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