RESULTS: Generally, patients had high expectations that they would benefit from GTT (M = 2.81 on 0-4 scale) and positive attitudes toward it (M = 2.98 on 0-4 scale). Patients also had relatively poor knowledge about GTT (48% correct answers on an objective test of GTT knowledge). Greater expectations for GTT were associated with lower knowledge (b = –0.46; p < .001), more positive attitudes (b = 0.40; < .001), and lower education (b = –0.53; < .001). DISCUSSION/SIGNIFICANCE: This research suggests patients have high expectations that they will benefit from GTT, which is associated with low knowledge, positive attitudes, and low education. Interventions may be needed to boost understanding and moderate expectations, particularly for disadvantaged patients.

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MYC Inhibition Overcomes IMiD Resistance in Heterogeneous Multiple Myeloma Populations†

Lorraine Davis[1], Zachary J. Walker[1], Denis Ohlstrom[2], Brett M. Stevens[3], Peter A. Forsberg[3], Tomer M. Mark[3], Craig T. Jordan[3] and Daniel W. Sherbenou[3]
[1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]Emory University, Atlanta, GA and [3]University of Colorado Anschutz Medical Campus, Aurora, CO

OBJECTIVES/GOALS: Immunomodulatory drugs (IMiDs) are critical to multiple myeloma (MM) disease control. IMiDs act by inducing Cereblon-dependent degradation of IKZF1 and IKZF3, which leads to IRF4 and MYC downregulation (collectively termed the "Ikaros axis"). We therefore hypothesized that IMiD treatment fails to downregulate the Ikaros axis in IMiD resistant MM. METHODS/STUDY POPULATION: To measure IMiD-induced Ikaros axis downregulation, we designed an intracellular flow cytometry assay that measured relative protein levels of IKZF1, IKZF3, IRF4 and MYC in MM cells following ex vivo treatment with the IMiD Pomalidomide (Pom). We established this assay using Pom-sensitive parental and dose-escalated Pom-resistant MM cell lines before assessing Ikaros axis downregulation in CD38+CD138+ MM cells in patient samples (bone marrow aspirates). To assess the Ikaros axis in the context of MM intratumoral heterogeneity, we used a 35-marker mass cytometry panel to simultaneously characterize MM subpopulations in patient samples. Lastly, we determined ex vivo drug sensitivity in patient samples via flow cytometry. RESULTS/ANTICIPATED RESULTS: Our hypothesis was supported in MM cell lines, as resistant lines showed no IMiD-induced decrease in any Ikaros axis proteins. However, when assessed in patient samples, Pom treatment caused a significant decrease in IKZF1, IKZF3 and IRF4 regardless of IMiD sensitivity. Mass cytometry in patient samples revealed that individual Ikaros axis proteins were differentially expressed between subpopulations. When correlating this with ex vivo Pom sensitivity of MM subpopulations, we observed that low IKZF1 and IKZF3 corresponded to Pom resistance. Interestingly, most of these resistant populations still expressed MYC. We therefore assessed whether IMiD resistant MM was MYC dependent by treating with MYCi975. In 88% (7/8) of patient samples tested, IMiD resistant MM cells were sensitive to MYC inhibition. DISCUSSION/SIGNIFICANCE: While our findings did not support our initial hypothesis, our data suggest a mechanism where MYC expression becomes Ikaros axis independent to drive IMiD resistance, and resistant MM is still dependent on MYC. This suggests targeting MYC directly or indirectly via a mechanism to be determined may be an effective strategy to eradicate IMiD resistant MM.

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Transcriptomics for gallbladder cancer prognosis

Linsey Jackson[1], Loretta K. Allotey[2], Kenneth Valles[2], Gavin R. Oliver[3], Asha Nair[3], Daniel R. Obrien[3], Rondell P. Graham[4], Mitesh J Borad[5], Arjun Athreya[6] and Lewis R. Roberts[2]
[1]Mayo Clinic, [2]Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, and Mayo Clinic Cancer Center, Rochester, MN, USA, [3]Department of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN, USA, [4]Department of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine, Rochester, MN, [5]Department of Hematology/Oncology, Mayo Clinic College of Medicine, Phoenix, AZ and [6]Department of Pharmacology, Mayo Clinic College of Medicine, Rochester, MN

OBJECTIVES/GOALS: Recent research has attempted to identify diagnostic, prognostic, and predictive biomarkers, however, currently, no biomarkers can accurately diagnose GBC and predict patients prognosis. Using machine learning, we can utilize high-throughput RNA sequencing with clinicopathologic data to develop a predictive tool for GBC prognosis. METHODS/STUDY POPULATION: Current predictive models for GBC outcomes often utilize clinical data only. We aim to build a superior algorithm to predict overall survival in GBC patients with advanced disease, using machine learning approaches to prioritize biomarkers for GBC prognosis. We have identified over 80 fresh frozen GBC tissue samples from Rochester, Minnesota, Daegu, Korea, Vilnius, Lithuania, and Calgary, Canada. We will perform next-generation RNA sequencing on these tissue samples. The patients clinical, pathologic and survival data will be abstracted from the medical record. Random forests, support vector machines, and gradient boosting machines will be applied to train the data. Standard 5-fold cross validation will be used to assess performance of each ML algorithm. RESULTS/ANTICIPATED RESULTS: Our preliminary analysis of next generation RNA sequencing from 18 GBC tissue samples identified recurrent mutations in genes enriched in pathways in cytoskeletal signaling, cell organization, cell movement, extracellular matrix interaction, growth, and proliferation. The top three most significantly altered pathways, actin cytoskeleton signaling, hepatic fibrosis/hepatic stellate cell activation, and epithelial adherens junction signaling, emphasized a molecular metastatic and invasive fingerprint in our patient cohort. This molecular fingerprint is consistent with the previous knowledge of the highly metastatic nature of gallbladder tumors and is also manifested physiologically in the patient cohort. DISCUSSION/SIGNIFICANCE: Integrative analysis of molecular and clinical characterization of GBC has not been fully established, and minimal improvement has been made to the survival of these patients. If overall survival can be better predicted, we can gain a greater understanding of key biomarkers driving the tumor phenotype.

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Rib Fractures in Geriatric Trauma: A Review of 1,037 Cases at a Single Level I Trauma Center

Forest Sheppard[1], Joseph D. Mack[2], Carolyne Falank[1], Bryan C Morse[1], Daniel C Cullinane[1], Joseph F Rappold[1], Julianne Ontengco[1] and David Ciraulo[1]
[1]Maine Medical Center and [2]University of Tennessee

OBJECTIVES/GOALS: Rib fractures are common traumatic thoracic injuries and are associated with high rates of morbidity and mortality. In those age â‰¥ 65, the rate of these complications double. This study sought to identify the extent to which injury-related predictors influence

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clinical outcomes in geriatric patients with rib fractures. METHODS/STUDY POPULATION: A retrospective 5-year review was performed of a single Level 1 Trauma center registry. Geriatric patients (â‰¥65 years of age) diagnosed with rib fractures from January 1, 2014 to December 31, 2019 were included. The primary outcome of interest was in-hospital mortality. Secondary outcomes included hospital and intensive care unit length of stay (HLOS and ICU LOS, respectively) and discharge disposition, as a surrogate for loss of independence. Further, subgroup analysis based on number of rib fractures (i.e. <4 and â‰¥4 rib fractures) was performed. RESULTS/ANTICIPATED RESULTS: 2,134 adult trauma patients were admitted with at least one rib fracture. Of these, 1,037 (49%) were â‰¥ 65 years old. This cohort had a mean age of 78.6 years old, injury severity score (ISS) of 11.4, HLOS of 7.4 days and 29% required ICU care with mean ICU LOS of 1.9 days. Only 36% were discharged home compared to 64% who were discharged to a care facility and thus had a loss of independence. Overall mortality was 6.3%. Compared to survivors, non-survivors had a higher ISS (19.3 vs. 10.8, $p = < 0.0001$) and longer ICU LOS (7.1 vs. 6.5 days, $p = 0.04$). Analysis based on number of rib fractures showed that those with â‰¥4 rib fractures had significantly higher mortality (8% vs. 4%, $p = 0.008$), longer HLOS (8.7 vs. 6.1 days, $p < 0.0001$), longer ICU LOS (2.6 vs. 1.3 days, $p < 0.0001$), and significantly lower discharge to home (32% vs. 39%, $p = 0.02$). DISCUSSION/SIGNIFICANCE: To our knowledge, this is the largest single-center study of geriatric patients with rib fractures. In this study, the observed mortality in patients â‰¥65 years of age was 6.3% which represents a lower mortality rate than historically reported. Despite this, only 36% were able to be discharged directly to home.

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Developing a Digitally Integrated Endotracheal Tube for Neonates to Improve Safety and Respiratory Function

Thomas Nienaber[1], Sarah Perez[2], Krista Stephenson[3], Joseph Sanford[4], Adria Abella[5], Morten Jensen[6] and Kevin Sexton[7]
[1]University of Arkansas for Medical Sciences, [2]UAMS/ACH Neonatology, [3]UAMS/ACH Pediatric Surgery, [4]UAMS Anesthesia/Clinical Informatics, UAMS Institute for Digital Health and Innovation, [5]UAMS Institute for Digital Health and Innovation, [6]University of Arkansas Bioengineering and [7]UAMS Surgery/Informatics, Institute for Digital Health and Innovation

OBJECTIVES/GOALS: Neonatal endotracheal tubes (ETTs) are usually uncuffed to avoid subglottic stenosis and other complications, but cuffed ETTs allow better ventilation. Our goal was to detect and control pressure in the cuff below the limit of occluding venous flow to minimize the risk of subglottic stenosis. METHODS/STUDY POPULATION: We designed a pressure sensor to fit on a 2.5 ETT for prototype testing in 8 age adult female rabbits. Eight uncuffed age- and sex- matched rabbits served as control. Study duration was 2 hours during which pressure in the cuff was limited by novel sensor (intervention) or auscultation (control). Anesthesia was maintained with sevoflurane. Ventilation was provided mechanically. Subsequently the tracheae were removed, sectioned crosswise, and compared histologically for mucosal damage. RESULTS/ANTICIPATED RESULTS: Preliminary data demonstrated an almost 30% greater amount of intact mucosa in the intervention group. The sensor also provided data on heart rate and respiratory rate, although this signal was not optimal. After filing an invention disclosure and provisional patent, we are refining our device to include multiple compartments for local control of cuff pressure and applying for a STTR Phase I/II application. DISCUSSION/SIGNIFICANCE: Ventilation in neonates with uncuffed ETTs can be suboptimal due to leak around the tube, but cuffed ETTs pose the threat of subglottic stenosis and other complications. We have designed a prototype cuffed ETT with a sensor to maintain low cuff pressure while preventing leaks and largely avoiding damage to the tracheal mucosa.

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Biobehavioral predictors of dose-limiting toxicities of cancer therapy: Identification of areas for preventative intervention†

Clifton P. Thornton[1] and Kathy Ruble[1]
[1]Johns Hopkins University

OBJECTIVES/GOALS: This presentation outlines a novel approach to evaluating multiple risk factors for the development of dose-limiting toxicities in adolescents and young adults with cancer. This is the first to evaluate biobehavioral predictors originally identified in animal models in clinical human studies. METHODS/STUDY POPULATION: Adolescents and young adults (AYAs) have seen the slowest improvements in cancer survival and have some of the highest rates of dose-limiting mucositis (mouth sores). AYAs receiving chemotherapy with a significant chance of dose-limiting mucositis were recruited for a prospective study. Baseline perceived psychologic stress levels and inflammatory markers were collected at the time of chemotherapy administration and participants completed a daily assessment of mucositis for 14 days following chemotherapy. Logistic regression will be used to evaluate stress and inflammation as predictors of mucositis and Sobels testing will evaluate the role of inflammation as mediators in this relationship. RESULTS/ANTICIPATED RESULTS: We anticipate that, as seen in animal models, stress and inflammation will predict mucositis development. First, we hypothesize that stress levels and inflammatory markers will have a direct correlation and that the level of inflammation at the time of chemotherapy administration will predict mucositis incidence and severity. Through mediation testing, we hypothesize that inflammatory markers will explain a significant amount of the variance in mucositis also explained by stress, identifying inflammation as a mediator in this relationship. In all, we expect that stress and inflammation both predict mucositis development and will be identified as important modifiable factors that can be altered to reduce the risk of toxicity development during cancer therapy. DISCUSSION/SIGNIFICANCE: This work intends to evaluate predictors of chemotherapy-related toxicity development in AYAs with cancer and identify areas of intervention that will reduce toxicity profiles and close the gap in cancer survival for AYAs. Findings are applicable to biomedical, nursing, and psychosocial professionals and will inform future, large clinical studies

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Exoskeletons increase paretic limb use in stroke survivors during a bimanual virtual reality reaching task*

Alexander Brunfeldt[1], Peter Lum[2] and Barbara Bregman[1]
[1]Georgetown University and [2]The Catholic University of America

OBJECTIVES/GOALS: Almost 8 million Americans live with disability caused by stroke. However, recent advances in stroke rehabilitation are costly and lack resemblance to activities of daily living. The goal of this study was to develop a rehabilitation platform to increase

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