and efficient adaptation to public health and other crises. RESULTS/ANTICIPATED RESULTS: The E-scan approach helped identify challenges, successful practices, and evidence-based strategies for building adaptive capacity and preparedness of CTSAs across various scientific sectors of the translational science spectrum. Some of the findings include: - Roadmaps for the creation of new collaborative research resources (biobanks; data repositories, etc.); - Rapid clinical and research decision making during public health crises; - New community-based research strategies to facilitate communication, research dissemination, and participant recruitment based on existing trust-based networks; - Innovative resource allocation to guarantee continuity of training and research opportunities for trainees. DISCUSSION/SIGNIFICANCE: The Environmental Scan of the Adaptive Capacity of CTSA hubs provides useful knowledge and tools to diverse clinical research stakeholders for mitigating the impact of a disaster via adjusting programs, practices, and processes, and building capacity for effective, emergency-ready and responsive research, training, and community engagement.

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Dysfunctional leukocyte mitochondrial metabolism is associated with immune paralysis in critically ill septic patients

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OBJECTIVES/GOALS: The host immune response during sepsis is now recognized to have anti-inflammatory pathophysiology. We aim to determine whether mitochondrial dysfunction of leukocytes predicts which critically ill septic patients develop immune paralysis and to identify differences in cellular metabolites between patients with and without immune paralysis. METHODS/STUDY POPULATION: Critically ill septic and control adult patients were recruited from one of 6 ICUs in a single-center tertiary care academic hospital. After enrollment, peripheral blood mononuclear cells (PBMCs) were isolated from a tube of whole blood on day 0-1 after ICU admission. Flow cytometry to quantify monocyte HLA-DR was performed to determine whether patients were immune paralyzed or not. Mitochondrial functional assays of PBMCs were performed with inhibitors of the electron transport chain to assess for differences in oxidative phosphorylation and glycolysis utilization. Metabolic profiling of cell pellets was performed to evaluate for specific metabolites and pathways associated with immune paralyzed patients. RESULTS/ANTICIPATED RESULTS: A total of 101 patients were recruited, including 62 control and 39 septic patients. 81 patients had immune paralysis status available for analysis. 52% of all recruited subjects were immune paralyzed. Of these, 58% were controls and 75% were septic. Immune paralyzed septic and control patients showed features of reduced utilization of oxidative phosphorylation (ox phos) including reduced basal respiration, ATP production and maximal respiration compared with non-immune paralyzed septic and control patients. Immune paralyzed septic patients showed diminished glycolysis utilization compared with septic non-immune paralyzed patients. Finally, cellular kynurenine and quinolinate levels were low in both immune paralyzed control and septic patients compared with non-immune paralyzed patients. DISCUSSION/SIGNIFICANCE: The PBMCs of immune paralyzed septic patients show evidence of mitochondrial dysfunction, with reduced ox phos and glycolysis utilization. Low levels of kynurenine and quinolinate, metabolite precursors to NAD+, in immune paralyzed patients may signal key deficiencies and targetable therapeutic avenues for reversal of an immune paralyzed state.

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A Novel High Dose Rate Brachytherapy Device for Preventing Local Recurrence of Pancreatic Cancer Dosimetry Verification

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OBJECTIVES/GOALS: To demonstrate safety and limit damage to off-target organs, we will be determining dosimetry parameters through experimentation and Monte Carlo simulations with our brachy therapy applicator designed to improve upon current designs to treat a 3-dimensional volume. METHODS/STUDY POPULATION: Low-cost materials were used to manufacture our High Dose Rate (HDR) applicator and a readily available after loading system was used to load our configuration with a radioactive source. The dosimetry of our device was analyzed using commercially available software and external beam therapy films to generate depth dose profiles and superficial dose distribution. Additionally, we attempt to confirm Task Group No. 43 (TG-43) dosimetry parameters using Monte Carlo simulations for our device. These data were compared with currently available applicators used for intraoperative radiotherapy. RESULTS/ANTICIPATED RESULTS: We anticipate that we will be able to validate dosimetry parameters for our device in preparation for clinical use. We aim to show our dose distributions align well with proposed target volumes while considering the composition and shape of our applicator. We hope to demonstrate that, unlike current applicators, our design is more effective at treating a 3-dimensional target volume. DISCUSSION/SIGNIFICANCE: By 2040, pancreatic cancer will be the second-largest cause of cancer-related deaths. Even with current brachytherapy applicators, 30-40% of pancreatic cancer seems to recur near the surgical site after surgery. By preventing local recurrence, we hope to improve patient outcomes.

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Convolutional Neural Networks and Machine Learning in the Identification of Ultrasonographic Features of Ovarian Morphology

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OBJECTIVES/GOALS: To develop a two-staged convolutional neural network to identify the ovary and antral follicles within ovarian ultrasound images and determine its reliability and feasibility compared to conventional techniques in 2D and 3D ultrasonography image analysis. METHODS/STUDY POPULATION: De-identified and archived ultrasonographic images of women across the reproductive spectrum (N=500) will be used in the study. These ultrasound images will be labeled by experienced raters to train a two-staged convolutional neural network (CU-Net). CU-Net will first separate the entire ovary from the background and subsequently identify all antral follicles within the ovary. Following

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training, the CU-Net will evaluate a second set of independent images (N=100) to determine performance accuracy. Three specialized raters will establish the reliability and feasibility of CU-Net compared to conventional 2D and 3D ovarian ultrasound image analysis methods. RESULTS/ANTICIPATED RESULTS: The labeled training dataset of ovarian ultrasound images is expected to successfully train the CU-Net and allow for accurate identification of the ovary and the total number of antral follicles in the second testing set of ultrasound images. When compared to conventional 2D and 3D ultrasound image analysis methods, CU-Net is expected to have similar accuracy when compared to the gold-standard method (2D-Offline with Grid) and outperform other approaches, such as 2D-Real Time and 3D volume software (VOCAL and Sono-AVC). However, CU-Net is anticipated to be the fastest and most reliable method across users, supporting its clinical feasibility. DISCUSSION/SIGNIFICANCE: This study will immediately translate to providing a standardized platform that can improve the accuracy, reliability, and time demand required for the evaluation of ovarian ultrasounds across users and clinical and research settings.

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Post-transcriptional regulation of the MiaA prenyl transferase by the small RNA CsrB in Escherichia coli (E. coli)

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OBJECTIVES/GOALS: MiaA is a highly conserved prenyl transferase that catalyzes synthesis of the i6A37 tRNA modification in E. coli. While transcriptional regulation of MiaA is well characterized, there is no information on the MiaA post-transcriptional regulation. The aim of this study is to characterize the post-transcriptional regulation of the MiaA gene in E. coli. METHODS/STUDY POPULATION: To characterize the post-transcriptional regulation of miaA, we executed a targeted genetic screen of an E. coli small RNA library on a miaA-lacZ translational reporter fusion strain to identify small RNAs (sRNAs) that modulate MiaA translation or transcription termination. We also measured MiaA mRNA levels and miaA-lacZ activity in the absence or over-expression of candidate sRNA regulators of MiaA. We also measured MiaA mRNA levels in the absence of RNaseE and PNPase, two enzymes involved in mRNA turnover. Finally, we measured the ability of purified recombinant CsrA to bind to the MiaA mRNA transcript in vitro. RESULTS/ANTICIPATED RESULTS: We identified the carbon sensing sRNA CsrB and its cognate protein interaction partner CsrA, as potential post-transcriptional regulators of MiaA. Over-expression of CsrB fully repressed miaA-lacZ activity and MiaA mRNA levels. The absence of CsrA resulted in a defective miaA-lacZ activity and a 10-fold decrease in MiaA mRNA levels. We also identified an increase in the MiaA mRNA half-life particularly in the absence of RNaseE. Our results demonstrate an additional layer of regulation for the miaA operon by the CsrA/CsrB protein-sRNA system. DISCUSSION/SIGNIFICANCE: MiaA is a highly conserved bacterial protein. Our data may represent phenomena in an array of bacteria that could be targeted by novel antibiotics. The human MiaA homologue, TRIT1, plays a role in mitochondrial disorders. We anticipate that information garnered from MiaA studies will elucidate TRIT1 function and its role in mitochondrial disorders.

Workforce Development

Contemporary Research Challenges

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Empowering the Participant Voice (EPV): Participant Feedback to Improve the Clinical Research Enterprise

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OBJECTIVES/GOALS: Six CTSA sites formed a collaboration to DEVELOP, DEMONSTRATE, AND DISSEMINATE new infrastructure to streamline collection and analysis of research participant feedback, using the Research Participant Perception Survey (RPPS), common standards, and customized REDCap-based tools, to improve the clinical research enterprise. METHODS/STUDY POPULATION: DEVELOP charter, consensus approach, core survey, deployment standards, data-use agreements; define meta-data, system requirements for the infrastructure, use-cases. Engage stakeholders for broad institutional and community input. Build RPPS/REDCap project, visual analytics Dashboard External Module, and Program Dashboard module for evaluation. Configure to use with Multilingual Module. DEMONSTRATE by implementing site-based use cases that reflect local priorities and span diverse populations, testing different methods of survey deployment (REDCap, patient portal, SMS) to showcase utility and flexibility. Generate data for local and inter-institutional benchmarking. Refine, then DISSEMINATE new infrastructure across the Consortium and REDCap community for broader testing and uptake. RESULTS/ANTICIPATED RESULTS: The project team refined the RPPS survey for inclusivity and mode of informed consent; defined standards for survey timing, sampling, and study metadata; configured the data dictionary in English and Spanish for use with the multi-lingual module ; developed tools for project evaluation. Stakeholder engagement identified themes of anticipated value and fears about feedback. We designed an At-a-Glance Dashboard to display survey results with detailed analytics and filters. A REDCap application programming interface will send de-identified site data to the EPV Consortium Database to support benchmarking. Full implementation began November 2021 and will scale in 2022. Dissemination to Consortium and REDCap users is ongoing through presentations and a project website (www.Rockefeller.edu/research/epv). DISCUSSION/SIGNIFICANCE: Direct feedback from representative populations about their experiences in research is essential to understand and resolve barriers to broad participation in research. Streamlined RPPS/REDCap infrastructure provides a platform for local and national benchmarking, and collection of actionable data to improve clinical research.

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