444

Team Science Competencies for Clinical Research Professionals: Determining Skills and Leveling Through a Modified Delphi Approach

Angela Mendell[1], Jessica Fritter[2], Nicole Summerside[3], Bernadette 'Candi' Capili[4], Nicole Exe[5], Laura Hildreth[1], Elizabeth J. Kopras[1], Joe Colagreco[4], Andrea Ronning[4], Kathryn Johnson[6], Christa Varnadoe-Rothman[7], Shirley Helm[8], Bob Kolb[9], Thomas Jones[2]
[1]University of Cincinnati [2]The Ohio State University [3]University of Washington [4]Rockefeller University [5]University of Michigan [6]Sinai Medical Center [7]Yale University [8]Virginia Commonwealth University [9]University of Florida Carolynn

OBJECTIVES/GOALS: Team science competencies are not well-defined for nonfaculty staff of Clinical Research Professionals (CRPs) who conduct research. Using an existing framework, our work has determined skills associated with team science competencies as related to CRPs. Our team also outlined examples of those skills on a fundamental, skilled, and advanced level. METHODS/STUDY POPULATION: The team consists of both CRPs and those working in the Team Science space. This team used a modified Delphi approach to determine the skills and leveling examples of each team science competency. The team broke into four groups and was assigned 3-4 competencies each. Each group determined skills needed to support (exhibit, promote) each competency and then described an example of this skill at the fundamental, skilled, and advanced levels. Once each group was finished with their assigned competencies, they were re-assigned to a different group for review and changes. Finally, team science and CRP experts reviewed the skills and levels. RESULTS/ANTICIPATED RESULTS: Our results are a rubric that defines 3-5 practical skills per described competency. These skills are needed to support and promote each competency as a CRP. An additional outcome from this work includes examples of each skill at the fundamental, skilled, and advanced levels in a CRP's career. Each leveled example is described in a concise, actionable way using Bloom's taxonomy. This rubric is meant to be easily understood, very useable and able to be used in conjunction with existing CRP competency frameworks. By using Bloom's taxonomy, we set the stage for future educational programming in Team Science skill-building for clinical research professionals. DISCUSSION/SIGNIFICANCE: Team science concepts and competencies have been increasingly integrated into translational science teams. However, team science competencies related to CRPs have remained largely undefined. Our work helps to define these competencies for CRPs in a practical way. Our rubric fills gaps in, and builds on, existing CRP competency frameworks.

445

The effects of dietary fiber based on fermentability and viscosity on phosphorus absorption and the gut microbiome in chronic kidney disease-mineral and bone disorder

Annabel Biruete[1], Neal X. Chen[2], Shruthi Srinivasan[2], Kalisha O'Neill[2], David Nelson[2], Kathleen M. Hill Gallant[3], Sharon M. Moe[2]
[1]Purdue University [2]Indiana University School of Medicine [3]University of Minnesota

OBJECTIVES/GOALS: To compare the effects of dietary fiber supplementation based on fermentability and viscosity on phosphorus fractional absorption and the gut microbiome in a rat model of chronic kidney disease-mineral and bone disorder (CKD-MBD). METHODS/STUDY POPULATION: 25-week-old Cy/+ male rats (CKD hereafter) will be randomly assigned to receive one of four fiber treatments (10% w/w each) based on fermentability and viscosity: 1) Cellulose (-fermentability, -viscosity), 2) inulin (+fermentability, -viscosity), 3) psyllium husk (-fermentability, +viscosity), or 4) pectin (+fermentability, +viscosity). Diets will be formulated with a semipurified diet containing 0.7% phosphorus. Treatments will last for 10 weeks, and rats will be euthanized at 35 weeks of age, where animals have reached kidney failure. Intravenous and oral 33P will be used for intestinal phosphorus fractional absorption and cecal/fecal samples will be obtained at euthanasia for microbiome assessment using shotgun metagenomics. RESULTS/ANTICIPATED RESULTS: Our preliminary data show that fermentable dietary fiber (inulin) impacted phosphorus homeostasis by increasing the circulating levels of fibroblast growth factor-23 (a bone-derived hormone that increases phosphorus excretion in urine) and lowering circulating levels of phosphorus in the Cy/+ male rat model of progressive chronic kidney disease. We hypothesize that dietary fiber impacts phosphorus absorption in gut microbiome-dependent and independent mechanisms. For example, fermentable fiber enhances the production of short-chain fatty acids, lowering the intraluminal pH, and enhancing mineral solubility and absorption. Meanwhile, viscous fibers may encapsulate minerals limiting their absorption if these fibers are non-fermentable. DISCUSSION/SIGNIFICANCE: Hyperphosphatemia, or high circulating phosphorus, is a major factor in the pathogenesis of CKD-MBD. Treatment of hyperphosphatemia is focused on reducing intestinal absorption. However, available therapies vary in their efficacy and focus on phosphorus absorption in the small intestine, ignoring the possible impact of the large intestine.

446

To Stay or Not to Stay: Multidisciplinary Collaboration After NSF Funding

Mohammed, S., Tirrell, B., Davis, C., Zhang, T., & Basore, C., Liao, X., & Miller, G
The Pennsylvania State University

OBJECTIVES/GOALS: NSF often requires cross-disciplinary team composition to be competitive for funding. To what extent do research teams have multidisciplinary authorships after they win an award, given that awards are not contracts? We examined the quantity and quality of multidisciplinary collaboration of NSF-funded teams before and after receiving their award. METHODS/STUDY POPULATION: Our sample was 150 PIs and Co-PIs (67% male) from 58 NSF-funded EAGER (EArly-concept Grants for Exploratory Research) grants between 2013 and 2019. Using publicly available information, we collected the number of conference papers, publications, and grants PIs/co-PIs produced with each other (all PIs and co-PIs in a team or a partial subset). Based on Ph.D. fields, we also cataloged whether the combination of PIs/co-PI authors on outputs represented unidisciplinary or multidisciplinary collaboration after their NSF award. Multidisciplinary collaboration consisted of multidivisional (Ph.D. disciplines across NSF divisions, e.g., political science and cognitive psychology) or multidirectorate (Ph.D. disciplines across NSF directorates, e.g., psychology and engineering) authorship. RESULTS/ANTICIPATED RESULTS: Of the 74% of PI and co-PI teams who collaborated after their EAGER award, almost 9 out of 10 chose to work with a collaborator from a different discipline, and almost 8 out of 10 chose to work with a researcher from an extremely diverse discipline from their own (e.g., computer science and psychology). Research on interdisciplinary teams largely emphasizes the challenges and problems they face

https://doi.org/10.1017/cts.2023.473

but the current research demonstrated that 90% of the sample chose to continue working together across disciplines after EAGER awards. Therefore, future research should dedicate more attention to the nontangible benefits members receive in interdisciplinary teams. Moreover, quality measures revealed higher H-indices for multidisciplinary than unidisciplinary journals and conferences. DISCUSSION/SIGNIFICANCE: Our archival results revealed that NSF EAGER grants are having their intended effect of being a catalyst for 1) continued multidisciplinary (and especially multidirectorate) collaboration) and 2) high-quality multidisciplinary publication and conference output. These results have contributed to NSF policy changes to reinstate the EAGER grant.

447

Characterization of the human iridocorneal angle in vivo using a custom design goniolens with OCT gonioscopy

Alessandra Carmichael-Martins, Thomas J. Gast, Stephen A. Burns, Brittany R. Walker, Brett J. King
Indiana University Bloomington

OBJECTIVES/GOALS: The trabecular meshwork (TM) and Schlemm's canal (SC), located within the iridocorneal angle (ICA), form the main outflow pathway and a major target for glaucoma treatments. We characterized the human ICA in vivo with Optical Coherence Tomography (OCT) imaging using a customized goniolens and a commercial OCT device (Heidelberg Spectralis). METHODS/STUDY POPULATION: Imaging these structures is difficult due to the optical limitations of imaging through the cornea at high angles. Therefore, a clinical gonioscopy lens was modified with a 12mm plano-convex lens placed on its anterior surface to focus light on the ICA structures, and capture returning light. Each subjects' eye was anesthetized with 1 drop of Proparacaine 0.5%. The goniolens was coupled to the eye with gonio-gel and it was held by a 3D adjustable mount. OCT volume scans were acquired on 10 healthy subjects. The linear polarization of the OCT was rotated with a half-waveplate to measure dependence of the ICA landmarks on polarization orientation. RESULTS/ANTICIPATED RESULTS: The TM was seen in 9 of 10 subjects. Polarization rotation modified the brightness of the band of extracanalicular limbal lamina (BELL) and corneoscleral bands due to the birefringent nature of the collagenous structures, increasing the contrast of SC. SC width was 99 ± 20Âµm varying in size over space, including a subject with SC narrowing in the inferior-temporal quadrant. DISCUSSION/SIGNIFICANCE: This clinically suitable gonioscopic OCT approach has successfully been used to image the human ICA in 3D in vivo, providing detailed characterization of the TM and SC as well as enhancing their contrast against their birefringent backgrounds by rotating the polarization of the imaging beam.

448

Establishing the efficacy of naturally occurring endocannabinoid-like substance in an in vitro model of Fragile X Tremor/Ataxia Syndrome (FXT/AS)

Collis Brown, Dr. Sonya Sobrian, Dr. Tamaro Hudson
Howard University

OBJECTIVES/GOALS: FXT/AS is a devastating, rare neurological syndrome that negatively impacts movement and cognition and is suspected to induce mitochondria dysfunction. Currently, no effective pharmacological treatments for FXTAS exist. The goal is to restore mitochondrial viability using endocannabinoid-like compounds in a cell culture model of FXTAS. METHODS/STUDY POPULATION: To establish a cell model of mitochondrial dysfunction, fibroblast baby hamster kidney (BHK-21) cell lines were treated with glucose oxidase (GluOx) at varying concentrations and times. Mitochondrial viability was assessed by the colorimetric Janus B Green Assay, which stains the mitochondria and enables assessment of cell numbers and the presence of oxygen in anchorage-dependent cell culture. Upon establishing this model of mitochondrial dysfunction, we next investigated the ability of three novel mitochondrial antioxidants (e.g., macamides) to protect mitochondrial viability. RESULTS/ANTICIPATED RESULTS: GluOx treatment of BHK-21 cells caused a dose- and time-dependent increase in oxidative stress. The data demonstrated significant disruption in the morphology of BHK-21 cells at a high glucose concentration, i.e., 40 nM, between 2 and 24 hours post-exposure. The morphology data were confirmed by the Janus B Green colorimetric assay. In examining the effects of glucose on mitochondrial viability, we demonstrated that at 15, 30, 35, and 40 nM, glucose significantly decreased mitochondria viability compared to the untreated, with 40 nM having the greatest effect. Under these conditions of mitochondrial dysfunction, co-incubation of the cells with the 0.5 uM MAM69 macamide attenuated the GluOx-induced increase in oxidative stress, with 0.5 uM MAM69 alone showing no effect on mitochondria viability. DISCUSSION/SIGNIFICANCE: This study illustrates the efficacy of macamides, natural occurring endocannabinoid like-compound, as novel prognostic and therapeutic candidates in the treatment of mitochondrial dysfunction that is associated with FXTAS. The use of BHK-21 fibroblast cells provides a rapid screening model to test for pharmacological therapeutic efficacy.

449

Progression of silica-induced pulmonary fibrosis is arrested after selective ablation of Col1a1+ fibroblasts

Daniel G Foster[1], Nomin Javkhlan[2], Jasmine Wilson[2], Benjamin L. Edelman[2], David W. H. Riches[2,3,4,5], Elizabeth F. Redente[2,3,4]
[1]University of Colorado Anschutz Medical Campus [2]Department of Pediatrics National Jewish Health, Denver, CO [3]Division of Pulmonary Sciences and Critical Care Medicine, Department of Medicine, Aurora, CO [4]Department of Pharmaceutical Sciences, School of Pharmacy, University of Colorado Anschutz, Aurora, CO [5]Department of Research, Veteran Affairs Eastern Colorado Health Care System, Aurora, CO

OBJECTIVES/GOALS: Silicosis is a highly fatal progressive fibrotic disease of the lungs characterized by accumulation and persistence of fibroblasts that excessively deposit Collagen1a1. We sought to eliminate Collagen1a1-expressing fibroblasts through a targeted genetic ablation strategy and hypothesized that this would arrest the progression of Silicosis. METHODS/STUDY POPULATION: Silicosis was induced with a single intratracheal (i.t.) instillation of silica particles (RESULTS/ANTICIPATED RESULTS: Targeted ablation of Col1a1 + fibroblast in established Silicosis resulted in a decrease in: 1) Col1a1+ fibroblasts by flow cytometry and within fibrotic nodules by immunofluorescent staining, 2) total lung collagen content by histology and hydroxyproline assay, 3) tissue-associated disease by microCT and an increase in arterial oxygen saturation by pulse oximetry. Cessation of targeted Col1a1+ fibroblast ablation resulted in a rebound effect in Silicosis disease progression. Following ablation, Col1a1+ fibroblasts expanded by proliferation (Ki67+) and total lung collagen levels returned to pre-ablation levels. DISCUSSION/

https://doi.org/10.1017/cts.2023.473