(virtual) testing will facilitate research during the covid-19 pandemic and are especially well-suited for data collection in rare disease populations.

Translational Science, Policy, & Health Outcomes Science

11979

Using whole-exome and mtDNA sequencing to develop a testing algorithm for diagnosis of mitochondrial disease in Puerto Ricans

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ABSTRACT IMPACT: Alterations in mitochondrial metabolism affect any tissue, especially those with the highest demand for energy. As the symptoms and clinical manifestations are heterogenous, disease diagnosis is challenging. The implementation of genetic-first approach in the diagnosis of mitochondrial diseases will expedite confirmation, treatment, management, and counseling of affected Puerto Rican individuals. OBJECTIVES/GOALS: Mitochondrial diseases are rare, and diagnosis is complex due to the heterogeneity of clinical manifestations. We aim to develop and implement a testing algorithm using a genetics-first approach, facilitating the identification of variants that contribute to mitochondrial disease's etiology and influence onset and progression in Puerto Ricans. METHODS/STUDY POPULATION: This is a cross-sectional study for characterizing clinical laboratory results from profiles used to evaluate metabolic diseases in individuals with suspected mitochondrial disorders from 2018 to 2021. A subset of 25 individuals from biochemical profile will be recruited to analyze their medical and family history, metabolic biomarkers in blood and urine, hearing test, imaging and chromosomal microarray. The implementation of a genetic testing algorithm using whole exome and mitochondrial DNA sequencing will be performed in a subset of 11 randomized individuals. Descriptive analysis will be reported, including a catalog of all variants. Multivariate analysis will be performed to estimate the statistical association between variants and phenotypes reported and adjusting for potential confounders. RESULTS/ANTICIPATED RESULTS: The biochemical profile of pediatric Puerto Rican individuals suspected of having mitochondrial diseases will be altered and can be used to differentiate among other metabolic causes. We expect to find altered levels of lactate, pyruvate and carnitines in serum, as well as altered organic acids in urine. The implementation of a testing algorithm using both, mitochondrial DNA and whole exome sequencing as first approach will be enabling the identification of disease-causing variants, thus enhancing and confirming the diagnosis of mitochondrial disease in Puerto Ricans. We will be able to identify rare/novel variants specific to our Hispanic population, for both nuclear and mitochondrial DNA. DISCUSSION/SIGNIFICANCE OF FINDINGS: This study will help to characterize the metabolic profile of pediatric Puerto Ricans. No previous study has been reported that describes testing algorithms for genetic diagnosis of mitochondrial disease in our population. Variants found will contribute to a deep understanding of the genetic contribution to phenotypes and disease susceptibility.

92811

Implementation of the Fitness, Lifestyle, and Optimal Wellness (FLOW) Program and Its Associated Health Outcomes

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ABSTRACT IMPACT: Through its interdisciplinary, tailored approach, the FLOW program could change the way that we approach promoting healthy lifestyle changes in the primary care field. OBJECTIVES/GOALS: The goal of this project is to assess patient outcomes associated with the implementation of the Fitness, Lifestyle, and Optimal Wellness (FLOW) Program. The ultimate aim of this program is two-fold: increasing patient-reported wellness and improving objective health measurements. METHODS/STUDY POPULATION: The FLOW program consists of a multidisciplinary team of sports medicine physicians, nutritionists, fitness trainers, and clinical psychologists. Patients who choose to participate in the program undergo a comprehensive physician-guided assessment, including lifestyle and metabolic evaluation, biomarker profile, and body composition analysis. Based on the patient's goals and results of evaluation, he/she is then connected with other members of the FLOW team to develop a comprehensive plan and offer resources for potential improvements in physical activity, nutrition, and/or behavior. The patient will undergo follow-up assessments and questionnaires at three and six months to track their objective measurements and reported progress. RESULTS/ANTICIPATED RESULTS: The anticipated results of the FLOW program are an overall improvement in patient health and wellbeing. More specifically, we anticipate seeing increased levels of exercise from initial reported levels, as well as better nutrition habits. We expect to see improvements in follow-up body composition assessments, with gains in fat-free mass and decreased body fat, in addition to patient-reported improvements in behavioral health as measured by PHQ-9, GAD-2, and the Perceived Stress Scale. We will also assess reported sleep health with the hopes to see improvement in follow-up assessments. DISCUSSION/SIGNIFICANCE OF FINDINGS: The FLOW program is designed to address health inequities that disproportionately affect the Deep South. Through this program, we propose a new role of the primary care team in promoting healthy lifestyle habits and disease prevention through exercise, nutrition, and behavioral health services.
Regulatory Science

Regulatory Science

Clinical Trial

95347

Examining the Impact of the BPCA: Promoting Pediatric Inclusion in Clinical Trials and Pediatric-Specific Drug Information

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ABSTRACT IMPACT: It provides insight in the relationship between pediatrics and clinical research and how pediatric

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participation in CT translates to clinical significance in form of drug labels, which inform clinicians on how to prescribe pediatric medications. OBJECTIVES/GOALS: Assessing the extent that the Best Pharmaceuticals for Children Act (BPCA) advances pediatric inclusion in clinical trials (CTs) and the availability of pediatric-specific drug information METHODS/STUDY POPULATION: The BPCA provides the U.S. Food and Drug Administration (FDA) authority to solicit sponsors whose drugs may benefit pediatric populations. Participation is voluntary and provides additional market exclusivity and pediatric information. CTs that received marketing exclusivity from 2016-2018 under BPCA were reviewed using Clinicaltrials.gov to access the legislation's impact. CTs were categorized according to eligibility: (1) pediatric and adult groups, (2) pediatrics, and (3) pediatric sub-groups. Studies were excluded for ambiguous age data. Studies open to both groups were evaluated for pediatric participation. Each drug was searched in DailyMed.com for published pediatric indications. RESULTS/ANTICIPATED RESULTS: Between 2016 - 2018, 22 drugs received marketing exclusivity under BPCA. Of the 196 CTs conducted for these drugs, 135 were available to adults and pediatrics, 10 were available to the entire pediatric population, and 51 were available to specific pediatric sub-populations. Exclusion criteria permitted only 118 of the CTs for assessment where eligibility included both pediatric and adult populations, of which 65 of these had less than 1% pediatric representation. Of the 22 drugs, 20 have pediatric indications. Over this three-year period, the number of CTs where adults and pediatrics were eligible were greater than CTs for pediatric only or pediatric subpopulations. DISCUSSION/SIGNIFICANCE OF FINDINGS: It is prevalent for BPCA compliant CTs to include both; 65% of drugs (13/20) with pediatric indications had more studies involving both groups than only pediatrics. Adequate pediatric CT representation is necessary for developing pediatric drug labeling with meaningful data for clinical indications.

Education/Mentoring/Professional and Career Development

81007

Training Biomedical Engineers in Regulatory Science: Critical Role of Experts from Industry and FDA

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ABSTRACT IMPACT: Lack of regulatory knowledge and education is a key barrier to the translation of medical devices and we describe the design and results for a university graduate-level course providing training on medical device regulatory submissions for approval that can help fill this unmet need and improve and accelerate translational success. OBJECTIVES/GOALS: Within the Indiana CTSI, the Medical Technology Advance Program (MTAP) in the Purdue University Weldon School of Biomedical Engineering (BME) offers three courses in regulatory science and regulatory affairs for medical devices. One course is focused on regulatory submissions for approval, and this report details the course design and evaluation. METHODS/STUDY POPULATION: For Fall 2020, the Regulatory Submissions for Approval course was enhanced to increase participation from regulatory professionals in US FDA and industry, with the core content, curriculum and course design led by BME faculty. The course was taught two days per week and included both in-person and remote (synchronous or asynchronous) attendance options. During the first class session each week a topic was covered in standard lecture format by BME faculty with industry regulatory experience. During the second class session, guests from both industry and FDA were invited to provide in-depth discussion on the topic, share perspectives and viewpoints, present real-world examples, experiences, and case studies, and answer student questions. An end of semester survey evaluated the effectiveness of the course design. RESULTS/ANTICIPATED RESULTS: Medical Device regulatory submissions and related activities were taught including product classification, presubmissions and meetings, 510(k), de novo, EUA, PMA, HDE, and advisory panels. FDA history, regulatory careers, regulatory science, and EU, China, and Japan regulations were also discussed. Overall, 29 speakers from FDA and industry participated live via video calls. A survey completed by 21/23 studentsrevealed overall satisfaction: all reported increased regulatory understanding and 20/21 learned 'a lot' or 'an incredible amount'. The weekly lecture was the top factor contributing to learning, and guest speakers were the next most important factors. Nearly all students indicated FDA and industry speakers were 'very' or 'extremely' valuable/helpful. Additional results will be presented. DISCUSSION/SIGNIFICANCE OF FINDINGS: The three courses are designed to improve medical device translation by training students to better understand regulatory processes and pathways. Survey results and feedback indicated this course was successful. Continued participation from FDA and industry is critical to the learning. Additional case studies will also help enhance learning.

Team Science

Basic Science

70274

TL1 team approach to investigating the adhesin gene fimH in adherent invasive E. coli induced inflammation and colorectal cancer development

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ABSTRACT IMPACT: We are developing the 3D perfusion system for use with patient-derived bacteria to further characterize the mechanism behind bacterial-induced inflammation and cancer. OBJECTIVES/GOALS: We previously reported the adherent invasive E. coli NC101 promote colorectal cancer (CRC) in mice. FimH, a mannose-specific adhesin on type 1 fimbriae, is involved in bacterial surface adhesion. Herein, we investigated the role of FimH in E. coli NC101-induced adherence and carcinogenesis in a novel 3D perfusion culture imaging plate. METHODS/STUDY POPULATION: E. coli NC101 gene fimH was deleted byï ¬Red Recombinase System. Biofilm formation was assessed by crystal violet and congo red staining. 5 dpf (wild-type strain) zebrafish embryos were infected in 6x107 cfu/ml wild type (WT) or fimH-deleted (ï „fimH) E. coli NC101 for 24hr and gut dissected for bacterial

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