Tufts CTSI Translational Science Day, 2023 Poster Session

*Indicates presenter

Poster #1

Title

Weight Management among Public Housing Residents Using Community Health Workers and Digital Technologies

Abstract

Purpose:

Making and sustaining improvements in diet and physical activity behaviors is challenging. A growing knowledge base documents the efficacy of community health worker (CHW) supported behavioral change interventions, recognizing CHWs' unique insights into how an intervention should be adapted to social and environmental contexts. There has also been expansion in the use of digital technologies for delivering health interventions. It is unclear if digital technologies alone are efficacious, or whether a more intense intervention consisting of a combination of CHWs plus digital technologies are needed to promote weight loss, particularly among individuals facing additional barriers (e.g., low income). This abstract describes the design of an ongoing 12-month randomized controlled trial to evaluate a Social Cognitive Theory-based intervention combining website-facilitated behavioral counseling from CHWs plus digital technologies (mHealth text message program and self-weighing via cellular connected scale).

Methods:

The study population are residents of Boston's public housing developments (low income, predominately identifying as members of minority racial/ethnic groups) with overweight or obesity (body mass index 27 or higher). Individuals (n=504) across public housing developments are randomized to 1 of 3 study groups: (1) CHW behavioral counseling plus mHealth text message program (CHW+mHealth), (2) mHealth only, and (3) an assessment only control group. The primary outcome is objectively measured weight loss at the 12-month follow-up. We hypothesize both CHW+mHealth and mHealth only will outperform the control group and that CHW+mHealth will outperform mHealth only. Secondary outcomes are changes in diet behaviors (via 24-hour recall) and objectively measured physical activity (via accelerometry). We are also assessing potential Social Cognitive Theory mediators (i.e., self-efficacy, motivation, outcome expectations) and moderating effects of participant characteristics and social contextual factors (e.g., access to health promotion resources).

Results/Findings:

This ongoing trial is currently recruiting the baseline cohort as well as conducting 6- and 12-month follow-ups; 184 individuals have been enrolled to date. Final results are anticipated in 2026.

Conclusions:

Results will inform our understanding of efficacious approaches to weight management among individuals living in public housing, which may be applied to other modifiable cancer-related behaviors and extended into the larger federal network of public housing administrations.

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Poster #2

Title

Modified Adiponectin mRNA Conjugated with Lipid Nanoparticles in Targeting Pathogenesis of Type 2 Diabetes

Abstract

Background: Type 2 diabetes (T2D) is a highly prevalent disease, in the US and worldwide, closely associated with genetics and lifestyles. Insulin resistance is a major factor in T2D development, and effective treatment for this condition is crucial to managing the disease and its associated risks.

Methods: This study presents a novel approach for treating T2D by the mechanisms of the inversely association of adiponectin (APN) level with insulin resistance and body mass index

(BMI). To enhance endogenous APN production in a diet-induced obese (DIO) mouse model, we utilized lipid nanoparticles (LNP) as safe delivery agents for APN mRNA conjugates.

Findings: Our results demonstrate that APN-mRNA-LNP administration induces APN synthesis in muscle, liver, kidney, pancreas, and fat cells. APN-mRNA-LNP treatment effectively reduces body weight and improves hyperglycemia. This treatment approach reactivates the Glut-4 gene to initiate glucose absorption. It decreases insulin resistance by activating DGKd, inhibiting DAG and PKCε, and deactivating insulin resistance. The inhibition of PKCε reactivates the insulin receptor, while activation of the Langerhans islets stimulates insulin secretion. Additionally, blocking the EGFR pathway alleviates diabetic nephropathy symptoms and reduces pro-inflammatory cytokines, TNF-a, IL-Ib and IL-6.

Interpretation: The APN-mRNA-LNP promotes APN enhancement in situ. Blood glucose levels and BMI are lowered as a result. Diabetic nephropathy symptoms and fatty changes in related organs are improved. It exerts these effects via distinct signal pathways. mRNA-LNP based nuclear acid therapy approves to be an effective and efficient approach in targeting the pathogenesis of T2D.

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Poster #3

Title

Multilevel Physical Activity Intervention for Low Income Public Housing Residents in the U.S.: Protocol for the Community Walks Trial

Abstract

Purpose:

Many physical activity behavioral interventions to change individual-level drivers of activity, like motivation, attitudes, and self-efficacy, are often not sustained beyond the intervention period. One possible cause of this lack of sustainability is that insufficient attention was paid to environmental factors that facilitate physical activity. A focus on interventions at both the environmental and individual levels might facilitate change in the long-term. This community-based study seeks to test a new multi-level (both environmental and individual levels), multi-component intervention to increase moderate intensity physical activity among people with low-incomes living in U.S. public housing developments, over a 2-year period.

Methods:

The design of this study is a prospective, cluster randomized controlled trial, with housing developments (n=12) as the units of randomization. In a four-group, factorial trial, we will compare an environmental intervention (E) alone (3 developments), an individual intervention (I) alone (3 developments), an environmental plus individual intervention (E+I, 3 developments), against an assessment only control group (3 developments). The E only intervention consists of community health workers leading walking groups, an advocacy program for residents, and provision of walking maps/signage. The I only intervention consists of a 12-week automated telephone program to increase physical activity motivation and self-efficacy. All residents are invited to participate in the intervention activities being delivered at their development. The primary outcome is moderate intensity physical activity measured by accelerometry among an evaluation cohort (n=50 individuals at each of 12 developments) at 2-year follow up. Mediation (e.g., neighborhood walkability, social support, motivation) and moderation (e.g., neighborhood stress) of our interventions will be assessed. Lastly, we will interview key informants to assess factors from the Consolidated Framework for Implementation Research domains to examine future implementation of multi-level physical activity interventions among public housing residents.

Results/findings:

This ongoing trial is currently recruiting the baseline evaluation cohort; 484 individuals have been enrolled to date. Final results are anticipated in 2025.

Conclusions:

Findings will inform whether a community-based multi-level approach will lead to sustained physical activity promotion over two years. If effective, this trial has the potential for implementation through other federal and state housing authorities.

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Poster #4

Title

A Translational Science approach to engineer a generalizable 3D tissue model of fibrotic diseases

Abstract

Tissue fibrosis affects millions of people and results in life-threatening loss of function in multiple organs. There is a significant unmet need for more *in vivo*-like tissue models to improve drug screening to treat fibrotic diseases. Our 3D tissue models for fibrosis in scleroderma delineates key principles to broadly develop a 3D tissue model that mimics fibrosis in other organs. By developing a generalizable protocol demonstrating conserved fibrosis mechanisms across organs,

our translational science approach will elucidate both scientific and operational principles needed to apply our 3D tissue model of fibrosis to multiple fibrotic diseases.

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Poster #5

Title

Exercise Capacity and Biomarkers of Inflammation and Remodeling in Individuals with Persistent Dyspnea, Fatigue and Exercise Intolerance after COVID-19

Abstract

Individuals recovering from COVID-19 may develop Post-Acute Sequelae of SARS-CoV-2 (PASC) lasting months to years beyond the original infection. Symptoms, quality of life scores, exercise physiologic variables, and blood biomarkers were measured in 25 study participants with persistent fatigue, dyspnea, and/or exercise intolerance (PASC-DFE) and were compared to 8 convalescent COVID-19 controls (CCC) and 8 healthy non-infected controls (HNC). Dyspnea and fatigue scores were higher while activity levels and quality of life scores appeared to be lower in the PASC-DFE cohort as compared to the CCC and HNC cohorts. In the 18 PASC-DFE participants who underwent cardiopulmonary exercise testing (CPET), the predominant pattern of limitation was an isolated circulatory impairment in 44.4% followed by dysfunctional breathing/hyperventilation in 16.7%. Levels of biomarkers of cardiovascular injury, remodeling, and inflammation are described for 41 participants presented to generate hypotheses on underlying mechanisms of disease.

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Poster #6

Title

Catalyzing Community and Stakeholder Engagement (CSE) across the Translational Spectrum through a Pilot Study Program

Abstract

Community and stakeholder engagement (CSE) is important for relevant and equitable clinical research but remains challenging. To inform effective CSE processes, Tufts CTSI interviewed fourteen principal investigators from different projects and a stakeholder from five of them. Inductive analyses revealed that CSE presented mutually beneficial outcomes, fostered by three facilitators. However, four challenges could hinder the development and sustainability of CSE. All investigators expressed intent to involve stakeholders in their other research studies, and stakeholders advised investigators to build authentic, sustained relationships. Investigators and stakeholders offered three additional recommendations for funders and research support organizations to deepen and expand CSE.

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Poster #7

Title

Antiphospholipid antibodies for the diagnosis of chronic Lyme disease

Abstract

Lyme disease is usually treated effectively with antibiotics. However, around 20% of patients continue to suffer symptoms even after treatment. The underlying cause of this chronic disease is unknown: it may be driven by an antibiotic-refractory infection, or by post-infectious immune dysregulation. The lack of a gold-standard diagnostic test for chronic symptoms impedes both basic and clinical research as well as patient care. Work at the Tufts Lyme Disease Initiative has identified an antibody marker of Lyme disease which correlates with post-treatment disease. Antiphospholipid antibodies are induced during acute infection and begin to decline after successful treatment of disease. We propose tracking the trajectory of antibody responses over time as a means to monitor patient response to therapy. This will provide proof-of-cure to most patients and a quantitative measure of chronic disease in others.

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Poster #8

Title

Critical Path Institute - Translating Data to Solutions: Accelerating Drug Development Through Public-Private Partnerships

Abstract

The Critical Path Institute (C-Path) leads collaborations that accelerate drug development, advancing better treatments for people worldwide. Established in 2004, C-Path plays a pivotal role in realizing the vision of FDA's Critical Path Initiative. By fostering a neutral environment, C-Path bridges pharmaceutical companies, academic researchers, and patient groups with regulatory agencies worldwide, embarking on high-impact, pre-competitive projects of highest public health interest. The Institute prioritizes regulatory and data science expertise to optimize innovative drug development tools and extend healthcare advancements.

C-Path's initiatives cover a broad spectrum of therapeutic areas, from common to rare diseases and from adult to pediatric conditions. Some of C-Path's key focus areas include Alzheimer's disease, Parkinson's disease, Huntington's, disease neonatal conditions, autoimmune disorders like Type 1 Diabetes, along with active efforts in addressing tuberculosis, asthma, depression, and other respiratory ailments.

C-Path is distinguished by its proficiency in crafting actionable solutions from data, termed as Drug Development Tools. These tools encompass biomarkers, clinical trial simulation tools, disease progression models, and patient-reported outcomes, gaining endorsements from regulatory bodies like the FDA and EMA. Consequently, academia and the pharmaceutical world have adopted them into their research. These tools have been instrumental in the approval of pioneering drugs for conditions such as Alzheimer's, Friedreich's Ataxia, Tuberculosis, polycystic kidney disease, and Type-1 diabetes.

A prime example of C-Path's collaborations is the International Neonatal Consortium (INC). This initiative unites a worldwide ensemble of experts and stakeholders—spanning the pharmaceutical industry, academia, patient groups, nursing communities, and regulatory agencies—to expedite the creation of safe and effective neonatal therapies. Together with the FDA, the INC has created a Real-World Data Analytics Platform (RW-DAP), housing patient data for over 350,000 neonates sourced from global electronic health records, clinical trials, and registries.

Looking ahead, C-Path is set on enhancing translational sciences, supporting FDA's regulatory science goals, and pioneering pediatric drug innovations. The institute is keen on advancing innovations in cellular and genetic therapies forward, leveraging artificial intelligence in drug development, and persistently valuing patient insights in their endeavors. Furthermore, a collaboration with Tufts Clinical and Translational Science Institute (CTSI) is on the horizon, aiming to harness the RW-DAP for refining clinical trial methods using historical controls in

neonatal studies. C-Path's guiding principle is clear: to lead and tackle significant drug development challenges.

In summary, C-Path continues to make strides in drug development, aiming for global improvements through its methodical approach, research-driven strategies, and versatile therapeutic endeavors.

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Poster #9

Title

Identifying Equity-Relevant Subgroup Effects in Alzheimer's Disease: A Literature Review to Support a Distributional Cost-Effectiveness Analysis

Abstract

Objective: Given the emergence of new therapies for Alzheimer's disease (AD), it is critical to understand the impact of access factors on heath equity. Distributional cost-effectiveness analysis (DCEA) can quantify tradeoffs between overall health gains and underlying impacts on health equity. Our objective was to support the development of a DCEA for AD by summarizing the existing literature across race, ethnicity, and level of social vulnerability.

Methods: We searched biomedical literature databases and grey literature for English-language studies that investigated AD outcomes of relevance for a DCEA, including AD prevalence, patient characteristics at diagnosis, disease progression measures, care setting, caregiver impact, and costs. We catalogued information by race, ethnicity, and level of social vulnerability (as measured by the Social Vulnerability Index).

Results: Our search yielded 8,744 references, of which we included 27 studies. We identified robust evidence for Black, White, and Hispanic subgroups related to AD prevalence and patient characteristics at diagnosis. For example, several studies reported higher prevalence and delayed timing of diagnosis among Black and Hispanic participants compared to White participants. Only two studies stratified data elements by level of social vulnerability. Few studies reported AD outcomes among Asian or Native populations.

Conclusion: There are sufficient data available to support a DCEA in AD. Robust estimates of AD epidemiology and timing of diagnosis will help us to understand the distributional impact of

emerging therapies. Further evidence and assumptions are needed to estimate impacts for some subgroups (e.g., Asian, Native, Social Vulnerability).

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Poster #10

Title

Intra-joint Sustained Release of Neosaxitoxin for Long-Term Osteoarthritis Pain Relief

Abstract

Osteoarthritis (OA) associated inflammatory activity often results in chronic pain for patients. Neosaxitoxin, a hydrophilic phycotoxin derived from Paralytic Shellfish Poison (PSP) and weighing 315.286 Da, is known to suppress neural pain signals by blocking sodium channels in nociceptors, making it a potential candidate for alleviating OA pain. However, its inherent high toxicity and rapid clearance from the synovial fluid mean that, at safe dosages, it only provides short-term pain relief. Poly (lactic-co-glycolic acid) (PLGA) is an FDA-approved biocompatible copolymer frequently used as a drug delivery system due to its controlled release properties. In this study, PLGA was incorporated with an additional FDA-approved hydrophilic material, Alginate, to formulate duo-core microparticles designed to consistently release small hydrophilic drugs. We hypothesize that using this formulation, a single dose of Neosaxitoxin can achieve a steady, non-toxic, and effective release rate over a month in vivo experiments. Ultimately, our goal is to provide long-term chronic pain relief for OA patients.

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Poster #11

Title

Programs, Resources & Services to Foster Collaborative, Interdisciplinary Research

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