Dr. Maureen Groer

THE PRETERM INFANT MICROBIOME: BIOLOGICAL, BEHAVIORAL AND HEALTH OUTCOMES AT 2 AND 4 YEARS OF AGE

Project Start Date: 13-MAY-2015
Project End Date: 29-FEB-2020

This project will follow 78 Very Low Birth Weight (VLBW) infants previously enrolled in a R21 grant through the age of 4 years. The data gathered over 6 weeks of the NICU stay includes multiple factors that potentially could alter the gut microbiome, such as prenatal and postnatal events and illnesses, amount of human milk received, weekly means of cytokines, chemokine's, growth factors and secretory Immunoglobulin A in the milk, and weekly levels of fecal calprotectin. Stool samples have been preserved for analysis of the micro biome in the current study. Micro biome species and diversities will be measured in the laboratory of Dr. Jack Gilbert at Argonne National Lab using state of the science deep sequencing and amplification of microbial sRNA genes. The micro biome will again be measured in stool samples from these children at the ages of 2 and 4 years. Relationship between the pre and postnatal factors, human milk volume and immunobiology, fecal calprotectin levels and the very early micro biome will be analyzed. The predictive power of the VLBW infant gut micro biome for determining later childhood micro biomes will be analyzed prospectively. The relationships between micro biomes across time and later growth, development and health will be determined. VLBW infants are at risk for both early and later health effects, and the role of the micro biome in these effects will be measured for the first time in this prospective study.

Dr. Cecile Lengacher

EFFICACY OF MBSR TREATMENT OF COGNITIVE IMPAIRMENT AMONG BREAST CANCER SURVIVORS

Project Start Date: 1-JUL-2015
Project End Date: 30-JUN-2020

Due to improved detection and treatment, survival rates among breast cancer survivors (BSC) have increased. However, BCS may experience cognitive impairment (CI) following treatment, which has been reported by BCS up to 10 years after chemotherapy (CT). There is limited evidence on whether stress- reducing interventions improve CI in BSC. The primary goal of this application is to establish the Mindfulness- Based Stress Reduction for Breast Cancer (MBSR(BC)) program as an effective treatment for CI in BCS. Specifically we aim to (1) evaluate the extent to which MBSR(BC) compared to the Breast Cancer-Education Support (BCES) program or Usual Care (UC) improves cognitive functioning among BCS off treatment; (2) determine if improvements in cognitive functioning achieved from MBSR(BC) are mediated through increased mindfulness and decreased rumination and stress; (3) evaluate genetic variants as moderators of MBSR (BC) on improvements in CI; and (4) determine the impact of MBSR(BC) on healthcare utilization and costs. To achieve these aims, we will conduct a randomized controlled trial (RCT) among 330 BCS with Stage I-III BC who have received adjuvant CT or CT and radiation. Within this RCT, MBSR(BC) will be delivered to a subpopulation of Spanish speaking BCS. Participants will be randomly assigned in a 1:1: 1 ratio to (1) the 6- week MBSR(BC) program; (2) the 6-week BCES program; or (3) UC. The BCES program will match the MBSR(BC) program for time and attention and parallel the group support component of MBSR(BC). Assessments will take place at baseline, 6 weeks, 12 weeks and 6 months and include clinical history and demographic information, objective neuropsychological assessments, subjective cognitive and symptom measurements, cost utilization surveys and a blood sample collection for genetic analyses. This study is highly innovative to be the first randomized controlled trial to: 1) evaluate the efficacy of MBSR(BC) among BCS for objective neuropsychological and subjective improvements in cognitive functioning; 2) evaluate genetic profiles as moderators of MBSR(BC) on improving CI; 3) offer the MBSR trial in Spanish in addition to English for the purpose of improving cognition; and 4) determine the effect of MBSR(BC) on CT- induced CI among BCS related to health service utilization costs. MBSR(BC) provides training to promote stress reduction through self-regulation of attention and awareness to stressful events. Our preliminary results show that MBSR(BC) improves subjective cognitive functioning. If MBSR(BC) is found to be effective, it will provide evidence of a viable non-pharmacological method for managing CI in BCS. Additionally, the examination of the effects of the hypothesized mediators may yield new insights for tailoring MBSR(BC) and/or developing additional interventions to aid BCS. The assessment of genetic polymorphisms to explore if risk alleles are associated with improvement in cognitive functioning may demonstrate that specific genetic profiles may modify improvements in CI for those receiving MBSR(BC). Finally, if MBSR(BC) is shown to be effective, this may significantly impact healthcare utilization and cost and produce necessary evidence for clinicians, researchers and policymakers.
**Dr. Maureen Groer**

**CHRONIC TOXOPLASMA GONDII, PREGNANCY REACTIVATION, AND PERINATAL DEPRESSION**

**Project Start Date:** 12-AUG-2017  
**Project End Date:** 31-MAY-2022

Project Summary/Abstract:

Toxoplasma gondii is a ubiquitous parasite that infects one third of the world's population. It remains in a latent state, encapsulated in cysts in the brain and muscle tissue of infected hosts. Reactivation rarely occurs, and usually only when the host has become significantly immunosuppressed. However, emerging literature suggests that chronic, latent infection is not innocuous. There have been reports associating depression, schizophrenia, suicidality, unusual behaviors, and migraine headaches with T. gondii IgG titers in chronically infected individuals. In addition, a few reports suggest that T. gondii can reactivate in healthy, immunocompetent pregnant women. These relationships have not yet been studied systematically in perinatal women. This proposal will study the relationships between latent T. gondii infection and depression through pregnancy and the early postpartum in T. gondii positive Hispanic women. Hispanic women are at highest risk for the type 1 serotype and a new highly virulent strain. Studies of behavioral and mood effects of T. gondii infection in both rodent models and humans have been done, but not in perinatal women. The research team has reported a relationship between T. gondii IgG titers and depression in second trimester pregnant women. In the proposed study, the role of socioeconomic and country of origin, cytokines, and immunosuppression will be determined across pregnancy. The relationship between IgG titer and depression in the postpartum will also be studied. A T. gondii negative control group will provide comparison. The second goal is to determine the true incidence of T. gondii reactivation in pregnant women with latent T. gondii infection. Women with positive IgG titers will be followed through pregnancy for changes in titer, symptoms, and for those with retinal scars, evidence of reactivation of chorioretinitis. The third goal is to explore the possibility of live tachyzoites transiting across the placenta into the fetal blood stream in T. gondii positive women.

**Additional Grant Info**

**Dr. Ponrathi Athilingam**

**I-CORPS: HEARTMAPP. A MOBILE APP FOR PATIENTS WITH HEART FAILURE**

**Start Date:** March 15, 2016  
**End Date:** August 31, 2016 (Estimated)

Heart failure is a significant public health problem. Currently there are over five million Americans, predominantly older adults, suffering from heart failure. These patients are expected to follow complex medication regimen and self-management practices at home to stay healthy and prevent getting admitted to hospitals. A mobile application (HeartMapp) is proposed to act as a health coach by reminding patients to follow health care providers' recommendations at home. Decision making on heart failure symptoms are often confusing and challenging for patients. The HeartMapp offers automated feedback to patients based on the patients' weight, heart rate, and symptoms entered in HeartMapp. Thus, patients are alerted when symptoms are mild to take the next step and prevent worsening and readmissions. Under new regulations, if these patients are readmitted within 30-days after discharge from hospital, the hospitals are not reimbursed, as well as penalized if the readmission rates are higher than a government set limit. Reducing readmission penalty for heart failure will provide financial benefit for health care organizations by generating revenue. Therefore, hospitals are also interested in finding ways to keep patients engaged in their self-management. In order to make HeartMapp available, this project needs to better understand the complex health care ecosystem, i.e., all the players in this market, the customers and the value that HeartMapp provides to them, the users and buyers and the approval process, and the revenue streams and resources needed to make it happen.

HeartMapp is an easy to use non-pharmacological, non-invasive application developed with five main features as intervention options: 1) assessment of daily weight, blood pressure, and chronic heart failure (CHF) symptoms with automated feedback to enhance decision making for management of symptoms; 2) exercise including physical activity (walking) and deep breathing to improve physical health and well-being; 3) real time vital signs monitoring utilizing a wearable Bluetooth device; 4) CHF info that includes audio enabled interactive CHF education to improve knowledge; and 5) Stats, a graphical module that displays trends on patient performance. From the technical standpoint, HeartMapp is currently available in the Android platform but it needs to be updated and enhanced to include the features...
coming out of this I-Corps project and translated into other software platforms (iOS and Windows) to expand the customer base. The current vision is to create a startup company or collaborate with an existing company to host the software and market the technology and license it to be included as part of existing solutions. The final report of I-Corps project will serve as a guiding document to: 1) submit a Phase I SBIR proposal in order to update the technology and test the HeartMapp for its efficacy in improving self-management of patients with CHF and thus potentially curb costly readmissions; 2) submit a Phase II SBIR proposal to take the technology to the market place; 3) Create a startup company or join an existing company interested in the commercialization of HeartMapp; and/or 4) find investors to provide the necessary funding to achieve our goals.

Dr. Kevin Kip

**ORAL CARE INTERVENTION IN MECHANICALLY VENTILATED ADULTS**

*National Institutes of Health*

**Start date:** 1-APR-2001  
**End Date:** 31-JUL-2018

Despite its prominent position in bedside care, there is little evidence to judge the benefits or associated risks of nurse-administered tooth brushing for mechanically ventilated adults, and the optimal frequency of tooth brushing in the critically ill has never been experimentally determined. This project will complete the examination of oral care interventions in mechanically ventilated adults with a randomized clinical trial of tooth brushing frequency (once, twice, or three times daily) focused on conclusively defining the benefit and risk of varied frequencies, and identification of moderating patient-level factors for risk and benefit. The project’s overall goal is to determine optimal tooth brushing frequency for mechanically ventilated adults. Optimal tooth brushing frequency is important for control of dental plaque and reduction of oral inflammation; it is likely to improve patient comfort, improve efficiency of nursing care, and may reduce systemic sequellae related to oral inflammation.

The primary aims of the proposed project are: 1) Evaluate the clinical equivalence (non-inferiority) of three tooth brushing frequencies on oral health (dental plaque and mucosal inflammation) in critically ill adults receiving mechanical ventilation; and 2) Quantify and compare the safety of three tooth brushing frequencies on serious adverse outcomes, including ventilator associated complications and clinically relevant HAIs. A secondary aim is to investigate patient factors that influence tooth brushing frequency benefit and risk in critically ill adults. These objectives will be accomplished using a prospective, randomized, experimental design. Subjects (n=345) will be randomly assigned within 24 hours of intubation to one of three intervention groups which differ in frequency of tooth brushing delivered by study personnel (once, twice, or three times daily). Dental plaque (UM-OHI score, with observations documented and augmented by use of a digital intraoral camera), mucosal inflammation (gingival crevicular fluid IL-1), and HAIs will be assessed daily during the intervention period. The data analysis will focus on providing definitive clinical practice guidance through joint evaluation of non-inferiority (comparison of dental plaque between groups by analysis of covariance) and quantification of number needed to harm. Repeated measures linear mixed models (treating dental plaque and mucosal inflammation as separate outcome variables) will provide insight as to specific patient-level factors that may modify the clinical effectiveness and safety profile associated with frequency of tooth brushing. Information about efficacy and safety of each frequency of tooth brushing will provide a clear recommendation for optimal tooth brushing frequency with direct translation to clinical practice.

Dr. John Clochesy

**PROMOTING CANCER SYMPTOMS SELF-MANAGEMENT IN OLDER ADULTS**

*Subcontract with UCF*

**Start Date:** 9/25/2015  
**End Date:** 8/31/2018

This research addresses the critical need to improve how older (= 65) adults self-manage side effects from cancer treatment such as chemotherapy induced nausea and vomiting (CINV). Older adults undergoing cancer treatment are at high risk for progressive severe effects resulting from nausea and vomiting. These effects include fluid and electrolyte imbalances, dehydration, muscle weakness, generalized fatigue, weight loss, dizziness, altered mental status, low blood pressure, changes in cardiac function, falls, and non-adherence with treatment plans. CINV is among the top five reasons why patients call their doctor while under treatment for cancer and has shown to lead to increased use of resources (e.g., unplanned emergency department (ED) and/or hospital admissions). Severe CINV related effects occur in up to 80% of older adults undergoing chemotherapy treatment resulting in high out-of-pocket costs. Additionally, quality of life (QOL) and daily functioning are greatly reduced with CINV. Guidelines exist for treating CINV; however, anti-nausea medications are often under-prescribed in the elderly and their use of self-management strategies at home is unknown. Research has
shown that older people with cancer are able to identify cancer-related symptoms such as CINV, but they are often not able to recognize the consequences of symptoms. This affects their ability to self-manage the symptom.

The goal of this project is to design, develop, and test an interactive “game” that will engage and prepare older adults to make self-care decisions related to CINV by allowing them to practice making self-care decisions for a character (avatar) in the game and visualizing the outcomes (positive or negative). The knowledge gained from playing the game will assist them in making better self-care decisions at home during or after chemotherapy treatment. This project will be conducted in two phases. Phase I will consist of designing and developing the game prototype to reflect real-life scenarios and experiences with CINV self-management. Older adults who have experienced CINV in the past, their caregivers, and oncology nurses will be included in the development team in order to create a game that is reflective of personal and professional experiences. Phase II will use a randomized clinical design to pilot test the game for feasibility and preliminary effectiveness in increasing self-manages behaviors, reducing CINV severity, and improving quality of life. Once shown to be effective, this novel educational strategy can be widely disseminated for use at the bedside and be adapted to educate older adults on self-management strategies for other cancer-related symptoms with negative outcomes.

Dr. Ming Ji

**PREDICTORS OF WEIGHT LOSS FAILURE AND REGAIN IN BARIATRIC PATIENTS**

*Subcontract with Kaiser Permanente Center for Health Research*

**Start Date:** 9/25/2015  
**End Date:** 7/31/2020

Although overall obesity rates are declining in the US, severe obesity (BMI > 35 kg/m2) is still increasing; rates are as high as 36% in some US ethnic minority populations. Bariatric surgery is the most promising treatment for weight loss in the severely obese, resulting in much higher excess weight loss (75% vs. 11%) than traditional behavioral methods. The most frequently used bariatric procedures (bypass and gastric sleeve) have clear evidence for durable weight loss, however, even within the same procedure type, weight loss varies substantially. For example, 25% - 50% of RYGB patients regain some of their initial weight lost within 3 years. We propose a unique, mixed methods, prospective cohort study to understand why some patients experience better weight outcomes than others. The healthcare
setting for this work, Kaiser Permanente Southern California (KPSC), performs ~3,500 bariatric surgeries annually; a larger target population for prospective research than any other single institution. Using socio-ecological, self-regulatory, and social cognitive theories for the basis of our study design, we propose to collect electronic medical record data and self-report surveys in 1,800 patients before surgery and at 12, 24, and 36 months post-operatively to examine demographic, behavioral, psychosocial, and perceived environmental predictors of weight loss/regain. We will also purposively select cross-sectional samples from 12-, 24- and 36-month survey respondents who do or do not achieve successful weight loss to participate in interviews and focus groups. We will test the following two main study aims and one exploratory aim: Aim 1. Over a 3-year follow-up period, determine how demographic, behavioral, psychosocial, and perceived environmental pre-surgical factors, and post-surgical behavioral and psychosocial factors predict a) the weight loss trajectory and b) weight loss success (defined as achieving and maintaining > 50% excess weight loss); Aim 2. Understand the variability in weight loss using qualitative methods in cross-sectional samples of post-operative survey respondents and use these findings to inform mediational models addressing Aim 1; Exploratory Aim 3. Over a 3-year follow-up period, study the development of adverse psychosocial consequences and determine how they relate to a) overall weight loss and b) weight loss success. Our study is designed to provide results that will move the science forward in two key areas: 1) optimizing patient selection in real-world settings for bariatric procedures using a better understanding of pre-operative predictors; and 2) program development for maximizing the benefits from surgery for the greatest number of people, using the knowledge we gain from studying mediators of post-operative weight loss.

< Return

**Dr. Theresa Beckie**

*I-CORPS: HERHEART*

*National Science Foundation Innovation Corps Teams Program (I-Corps Teams)*

**Tentative Start Date 6/15/2016**

**Tentative End Date 12/31/2016 (6 months)**

Coronary heart disease (CHD) afflicts nearly 7 million US women annually and remains their leading morbidity and mortality threat. Of these, 2.7 million have a history of myocardial infarction (MI), and an estimated 262,000 women are hospitalized annually with an acute coronary syndrome (ACS). Within a year of a first MI more women than men will die. Compared with men, women with ACS and those after coronary revascularization have longer hospitalizations and higher in-hospital mortality and endure up to 30% more readmissions within 30 days after the index hospitalization. Cardiac rehabilitation (CR) is an essential component of comprehensive care after ACS, is internationally endorsed, is integrated in evidence based guidelines for women and reveals incontrovertible morbidity and mortality benefits. Although referral to CR is designated as a performance measure of healthcare quality after ACS, CR has failed to reach over 80% of eligible women in the last 3 decades. Patient-oriented, medical and healthcare system barriers variably account for poor CR attendance among women. Without health insurance, CR costs about $6000 and even with health insurance, women can endure co-insurance payments of up to $50 for each of the 36 CR sessions ($1800). With an increasing ageing population and increasingly more women living with symptomatic CHD, the effectiveness and accessibility of secondary prevention (SP) health services for these women have never been more important. Alternatives to center-based CR programs are nonexistent. Thus, after hospital discharge women struggle with disease self-management without the knowledge or behavioral skills to effectively improve their risk factors for a subsequent cardiac event. Mobile health (mHealth) technology can deliver evidence-based health information and behavior theory based behavior change strategies to help women engage in self-care to manage their risk factors. A mobile application (app), “HerHeart” is an innovative SP intervention for improving reach, reducing cost and time, and improving health outcomes for women with CHD wherever they live. Empowering women with tailored information, intuitive self-monitoring, and personalized goal setting and feedback will transform SP from a 3-month center-based program to a paradigm of life-long engagement in healthy behaviors.

< Return

**Dr. Maureen Groer**

*MICROBIOME AS POTENTIAL MEDIATOR IN PRETERM INFANT NEURODEVELOPMENT*

**Start Date 9/21/2016**

**End Date 8/31/2023**

Preterm infants account for 12% of births, but disproportionately account for 40% of children who have cerebral palsy (CP), 25% of children with hearing impairment and 35% of those with vision impairment. Thus optimizing neurodevelopmental outcomes for preterm patients would have significant impact on outcome numbers for all children. Neurodevelopmental potential of the preterm infant is influenced by (i) Gestational age (GA), (ii) events in the neonatal intensive care unit, and (iii) care in the home environment after NICU discharge. This proposal will focus on understanding events that increase or decrease the risk of developmental impairment after an infant has been born preterm at a given gestational age, not on the prior exposures of prenatal and social factors that may have increased the risk of preterm birth. For a given infant, factors that caused preterm delivery are complete and fixed. Our goal is to instead focus on factors that are prospectively modifiable from the time of birth through early childhood in order to optimize a given infant’s neurodevelopmental potential. We will follow infants in two environments through two epochs -- the neonatal intensive care unit (NICU) hospital course from birth to discharge and the home environment from NICU discharge through school readiness evaluation at four to six years of age. We will
investigate the microbiome as a potential biologic effector of clinical and environmental factors associated with neurodevelopmental outcome in these epochs.

Dr. Maureen Groer & Velda Gonzalez-Marrero

FATIGUE AND THE GUT MICROBIOME OF PATIENTS RECEIVING CHEMORADIOThERAPY FOR RECTAL CANCER

Start Date 5/1/2017
End Date 4/30/20

Fatigue is one of the most distressing and commonly reported side effects of chemo-radiation (CRT), with up to 78% of rectal cancer patients complaining of severe fatigue during CRT. While the etiology and associated mechanism of the cancer-related fatigue during CRT treatment remain elusive, it has been suggested that dysbiosis (an imbalance in the intestinal microbiota in the gut) may contribute to worsening of fatigue during a patients’ pelvic CRT. This study will contribute to address the knowledge gap in symptom research and the health literature by providing initial evidence of the biologic/gut microbial processes related to the relationship among CRT, dysbiosis, and fatigue in the rectal cancer population, so that more innovative and individualized interventions can be developed. The proposed research is guided by a model of chemotherapy-related side effects. The training plan was designed to allow the applicant to expand her theoretical knowledge and skills in symptom phenotyping and conducting bio-behavioral and microbiome research in order to meet the NRSA traineeship goals and launch a career as an independent nurse scientists. An experienced team of scientists will lead the research training plan as related to the following objectives: (1) to enhance her understanding of the science related to the proposed mechanism linking CRT-induced gut microbiome dysbiosis and fatigue; (2) to increase her understanding of the characterization of CRT-related fatigue phenotypes with patient biological and clinical data, and microbiome data collection techniques and analysis through a bedside-to-bench approach; (3) to obtain comprehensive training and knowledge in microbiome research including stool collection and processing, bacterial 16S rRNA amplicon sequencing, shotgun metagenomics analysis and interpretation of microbiome-derived metagenomics data; and (4) to improve scientific writing skills and building collaborations with experts in the field of bio-behavioral/symptom management/microbiome research to successfully publish in high-impact, peer-reviewed journals, and submit competitive grant applications. The training plan is for twenty four months and includes six core areas: didactic; interdisciplinary seminars; mentorship; laboratory training; research; and dissemination. The specific aims of the proposed study are to: Aim 1: Examine the temporal changes in diversity of the gut microbiome over the course of CRT of adults with localized rectal cancers. Aim 1a: To investigate whether the intensity of fatigue during CRT is associated with the gut microbial diversity changes during the course of treatment. Aim 2: Examine the temporal changes on the abundances of specific gut microbes of adults with localized rectal cancers over the course of CRT. Aim 2a: To investigate the associations between changes in the gut microbial abundance with changes in fatigue scores during the course of CRT. By focusing on the innovative investigation of the relationship between gut microbial changes and fatigue symptoms during CRT, this study aligns with the mission of NINR calling for studies on patient-centered bio-behavioral research that promote health and enhanced quality of life.

Dr. Cindy Tofthagen & Susan McMillan

ACCELERATED RESOLUTION THERAPY FOR TREATMENT OF COMPLICATED GRIEF IN SENIOR ADULTS

Start Date pending
End Date pending

Prolonged, complicated grief (PCG) is associated with increased risk of suicide, diminished physical and psychological health, and decreased physical, psychological, and role functioning among older adults. Grief interventions are primarily delivered by hospice organizations throughout the US. These programs are beneficial in the setting of normal grief; however, their usefulness for treatment of prolonged or complicated grief is limited and few treatment options exist for PCG outside of the 12 months of grief services that all Medicare-funded hospice organizations are required to provide. This uncontrolled, prospective study will examine accelerated resolution therapy (ART), a brief form of psychotherapy, as a treatment for PCG. Primary caregivers (age >60 years) of an immediate family member who died after enrollment in hospice, who indicate significant symptoms of PCG and psychological trauma, will receive 4-6 weekly sessions of ART. Assessment of grief, psychological trauma, sleep, anxiety, and depression will occur pre-treatment, at week 4, and at 1-month follow-up. As a secondary aim, we will examine changes in stress biomarkers salivary alpha-amylase and salivary interleukin 6, before and after ART. The data obtained will provide invaluable insight into potential dose of ART intervention, as well as anticipated outcomes.