

Exploring Risk and Determinants of Mental Health in Lesbian, Gay, and Bisexual Older Adults

A growing body of evidence has documented disparities in the mental health of older lesbian, gay and bisexual (LGB) adults. This includes a higher risk for mental health distress and depression in LGB adults compared to their heterosexual peers. Our study aims to better understand the mental health problems experienced by LGB adults in later life. We will also study whether certain health conditions and behaviors may increase or decrease risk of mental health problems. Data from the Kaiser Permanente's Research Program on Genes, Environment and Health (RPGEH) will help us to better understand these risks and identify health factors that may be important for the mental health of older LGB adults. Findings from this study will identify modifiable health factors that may have important for improving the health of older LGB adults. It will also contribute to our knowledge on potential treatment options. Findings can also help other researchers who are developing and testing ways to improve the mental health of LGB adults.

A role of the LRRK2 Gene on the Inflammatory Bowel Disease and Parkinson's Disease Comorbidity

Parkinson's Disease (PD) is a progressive movement disorder with resting tremor, affecting ~1%-2% of people ages 60 and older. Several mutations in a gene, LRRK2, have been linked to the development of PD. Recently, LRRK2 mutations have been found in patients with inflammatory bowel disease (IBD), a chronic disorder of the digestive tract leading to diarrhea, pain, fatigue and weight loss. Nearly 1.3% U.S. adults are affected, most diagnosed before age 30. A recent study has shown that IBD patients are at a higher risk of developing PD compared to the general population. However, currently, there is no way to identify individuals with IBD who will develop PD. Therefore, we are proposing a study that will utilize the Kaiser Permanente Health System to develop genetic and clinical biomarkers of PD. Specifically, we will determine the mutation status of patients with IBD+PD at LRRK2 and other genes and will characterize clinical features of IBD patients that developed PD. Given a much earlier age of onset of IBD, a better understanding of the genetic and clinical factors predisposing IBD patients to PD would allow developing early biomarkers of PD development and identify new ways to treat or prevent PD.

Genetic associations with infection susceptibility and outcome

Sepsis is the leading cause of inpatient mortality, killing 250,000 people in the US each year. However, it is unclear why some people recover, and others develop septic shock or die. We aim to study how underlying patient genetics may affect whether a person becomes hospitalized with sepsis and how well they recover in response to treatment. By understanding these differences, we hope to improve opportunities for tailored treatment and improved sepsis survival. Using a genome-wide association study approach, we will look for differences in genetic patterns between people who do and who don't develop sepsis, and between people who respond and do not respond to treatment. By identifying these genetic differences, we will understand more about the biological systems involved in sepsis, and how new treatments can be developed and targeted to patients with particular genetic and clinical features. We hope that Kaiser Permanente members, and all people, who contract sepsis will benefit from treatment breakthroughs made possible by this research.

Identification of New Persistent Opioid Users After Surgery in the Genetic Epidemiology Research in Adult Health and Aging (GERA) Cohort

Long-term opioid use after surgery has become a concerning postoperative complication. In this pilot project (BHA&ID Section - 2019), we aim to collect preliminary data for an external grant which will aim to determine the genetic factors that increase one's susceptibility to develop persistent opioid use after surgery and to evaluate potential causal risks factors of this postoperative complication. Better understand the reasons why some patients continue to use opioids long after surgery is crucial to

develop personalized interventions prior to surgery and to consider alternative to opioid pain relief after surgery for at-risk patients.

Cannabis use in cancer patients: a growing exposure

This study will provide important information about the scope of cannabis use in cancer survivors across multiple regions of the U.S. It will also tell us if research participants are likely to be honest when reporting cannabis use in studies, as well as provide important preliminary evidence about whether or not cannabis use could be an alternative to opioids for cancer pain and other symptom management. With the growing accessibility of cannabis to individuals in the cancer patient and survivor communities, there is a strong and timely need to understand the cannabis use patterns in cancer patients. This work will help inform future research to improve the quality of treatment and symptom management for patients with cancer and will yield information that can be used to guide decisions regarding cannabis use for the growing population of cancer survivors who may now have legal access to marijuana. Overall, the proposed project is an efficient and important step in furthering our understanding of the factors that are important to cancer survivors and forms a solid foundation for extending our research into longer-term translational work and intervention.

Optimizing lung cancer risk stratification through prediction of lung cancer screening eligibility and family history of lung cancer

The National Lung Cancer Screening Trial (NLST) reported that screening with low-dose computed tomography (LDCT) reduced lung cancer mortality by 20%, and the US Preventive Services Task Force recommends yearly screening LDCT for 55- to 80-year-olds with 30+ pack-years smoking history who are current smokers or who quit in the last 15 years. Health systems have begun to implement lung cancer screening (LCS), but uptake remains low. This may be due in part to the inability of health systems to determine LCS eligibility across their membership. While documentation of smoking in electronic health records has improved, data capture is often incomplete. This hampers efforts to target eligible members and offer them LCS. It may also be important to characterize other risk factors for lung cancer, including lung cancer family history. We propose to use KPRB survey data as a gold standard assessment of LCS eligibility and lung cancer family history. We will then develop algorithms that use electronic health records data to predict LCS eligibility and lung cancer family history and use these in a lung cancer risk prediction model. This will improve the ability of health systems to conduct LCS.

Investigating the effects of KIR and HLA gene polymorphisms on psoriasis in the Kaiser Permanente RPGEH cohort

This project will investigate how genes encoding receptors on the surface of immune cells known as killer cell immunoglobulin-like receptors (KIR) interact with genes encoding antigen presenting molecules known as human leukocyte antigen (HLA) in the development of psoriasis, a common inflammatory disorder of the skin, nails, and joints that affects approximately 3% of the US population. There is also evidence that psoriasis affects the entire body, with links found between psoriasis and myocardial infarction, stroke, type 2 diabetes, and obesity. A key limitation in studying the role that KIR and HLA play in psoriasis is the time and expense of directly typing these genes. We propose to overcome this limitation by implementing statistical and machine learning algorithms to accurately estimate KIR and HLA genes in about 3,500 psoriasis patients and 10,500 healthy control patients from the Kaiser Permanente Research Program on Genes, Environment, and Health. We expect that the results of this project will improve the lives of psoriasis patients by aiding physicians and researchers in identifying individuals with heightened risk for disease and developing novel therapeutics for those patients with specific combinations of KIR and HLA genes that do not respond favorably to current therapeutics.