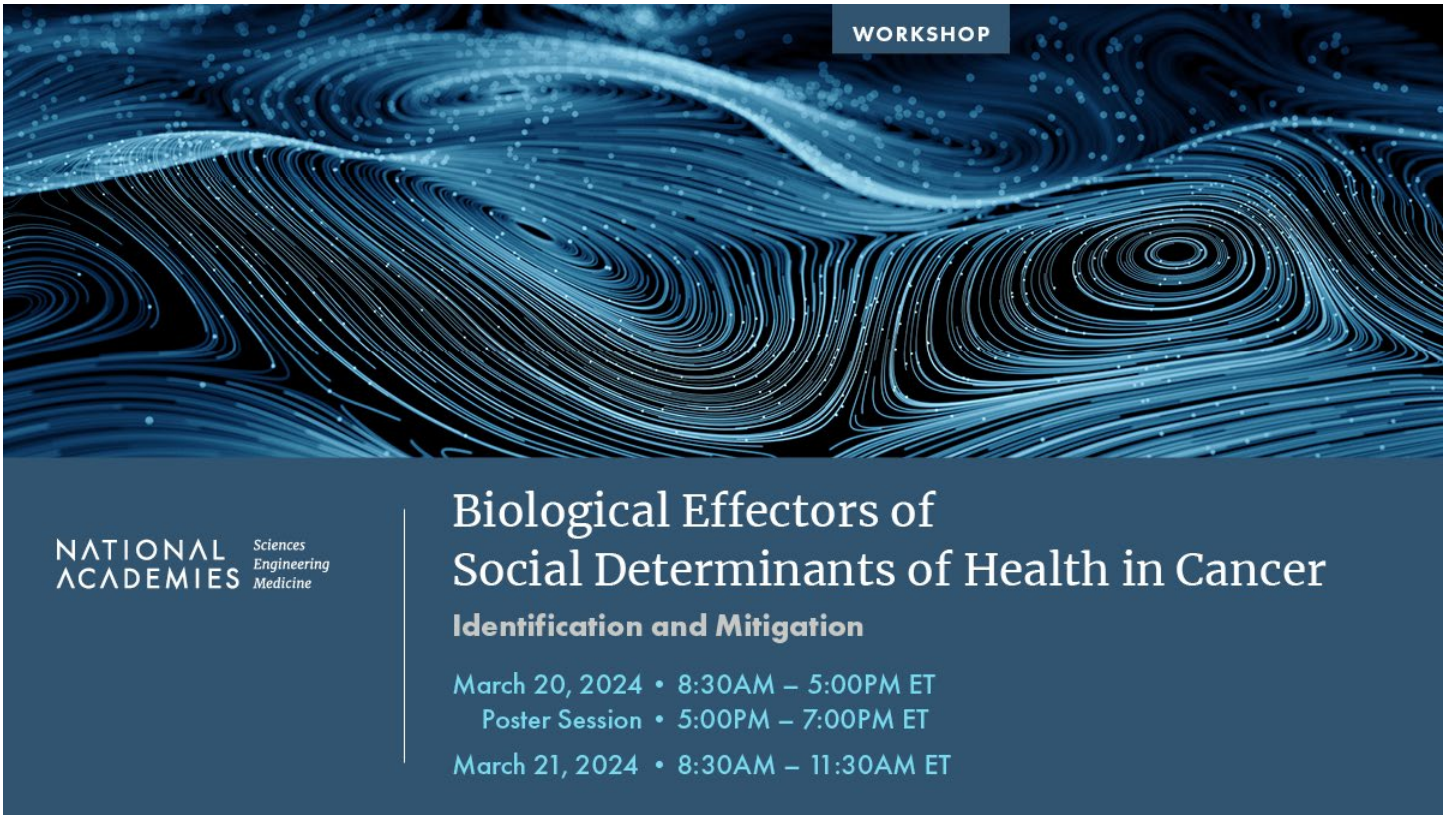
POSTER ABSTRACTS



The poster session will take place during the workshop reception:
Wednesday, March 20, 2024, from 5:00pm to 7:00pm ET

Find the poster PDFs archived online at
www.nationalacademies.org/biological-effectors-of-SDOH

Title: Genetic Ancestry and Epigenetic Age in Colorectal Tumors from The Cancer Genome Atlas

Authors:
Christopher L. Benson II[1,2] (presenting author), Marco Matejcic[2], Fredrick R. Schumacher[1,3], Stephanie L. Schmit[2,3]

[1]Department of Population and Quantitative Health Sciences, Case Western Reserve University, [2]Genomic Medicine Institute, Cleveland Clinic, [3]Population and Cancer Prevention Program, Case Comprehensive Cancer Center

Abstract:
Colorectal cancer (CRC) is the third most diagnosed cancer in individuals living in the United States and the third leading cause of cancer-related deaths in men while fourth in women. Among racial/ethnic populations, American Indian/Alaska Natives and Blacks have the highest rate of CRC. Utilizing publicly available data on 311 CRC cases from The Cancer Genome Atlas (TCGA), we examined the association between global genetic ancestry and epigenetic age (i.e., biological age) among CRC patients. Proportions of African (AFR), Admixed American (AMR), East Asian (EAS), and European (EUR) global ancestry were estimated using ADMIXTURE software. We performed a compositional data analysis using an additive log ratio transformation, where the individual ancestral components (i.e., AFR, EAS, NAT) were expressed in terms of additive log ratios with respect to a fixed reference component. Beta values were generated from the DNA methylation (DNAm) array data on primary tumor samples, and these values were used to estimate their epigenetic ages using two epigenetic clocks. The PhenoAge/Levine method estimated epigenetic age using the ENmix package, while epiTOC estimated epigenetic age based on the relative stem cell division rate. We examined associations between epigenetic age for each clock and global genetic ancestry, using linear regression, after adjusting for age at diagnosis, sex, stage, and anatomical site (colon or rectum). The overall contribution of genetic ancestry to somatic mutational status was also tested through a 3-degree of freedom likelihood-ratio test (3-df LRT). We did not observe a statistically significant association between genetic ancestry and epigenetic age (p-value= 0.7737 (PhenoAge) and 0.731 (epiTOC)). Our next step is to test the associations between individual global ancestry proportions and epigenetic age in both tumors and normal tissue to determine if one or more components may be associated with epigenetic age.

Title: Differential gene expression in pancreatic neuroendocrine tumors among those living with adverse SDOH

Authors:
Andrea Gillis[1] (presenting author), Brendon Herring[1], Vinodh Srinivasasainagendra[2], Weisheng Chen[1], Rachael Guenter[1], Tiwari Hemant[2], Dai Chen[3], Herbert Chen[1], J Bart Rose[1], Upender Manne[4], Smita Bhatia[3]

[1]University of Alabama at Birmingham, Department of Surgery, [2]University of Alabama at Birmingham, School of Public Health, [3]University of Alabama at Birmingham, Department of Pediatrics, [4]University of Alabama at Birmingham, Department of Pathology

Abstract:
Background: There are known health outcome disparities among those with pancreatic neuroendocrine tumors (pNET) of minority race and those living with adverse social determinants of health (SDOH) (rurality, uninsured, unmarried) influencing overall survival compared to their peers. The potential biologic mechanism of these factors is unknown.

Methods: With IRB approval, we reviewed patients who underwent surgical resection for Grade 1 and 2 pancreatic neuroendocrine tumors (pNETs) at our institution between 2006-2022. We identified 11 black patients (based on self-identified race) and matched them to age, sex, and tumor grade white controls. Formalin-fixed, paraffin-embedded (FFPE) pNET specimens were demarcated and dissected to isolate cancer cells with supervision from a board-certified pathologist before RNA isolation. Sequencing was performed by Illumina NextSeq550 at 200 million read depth paired-end samples. GRCh38 transcriptome alignments were performed using Salmon and differentially expressed genes (DEGs) determined using DESeq2 after normalization. Significance was determined by FDR-adjusted p-value (q-value; qv) < 0.05 and log2 fold-change (log2FC) ≥ ±2.

From the gene enrichment analysis, we created a linear regression predicting adverse residential community SDOH including poverty, social vulnerability index, low educational attainment and uninsured neighborhood based on publicly available census data using geocoded patient billing address. Our final model controlled for confounding variables including patient age, gender, race, BMI, and smoking status.

Results: Of the 24 patients identified, median age was 57years, 18 were grade 1 pNET, 30% resided in neighborhoods below federal poverty level. We identified 48 DEGs between those patients living in adverse SDOH communities compared to those who were not. Differential expression was seen in tumor suppression (TMEFF2), cell membrane (MBLAC2), and inflammatory (DAPK1-IT1) pathways for patients living in high poverty, low educational attainment, and low insurance access neighborhoods compared to controls.

Conclusion: Significant biologic changes are seen in the epigenome of those living in neighborhoods characterized by adverse SDOH.

	Association of Gene Expression and adverse social determinants of health (SDOH)				
SDOH	Gene	t-statistic	p-value	B	SE
Poverty	PPM1K divergent transcript(PPM1K-DT)	5.28	1.30 E-07	18271.39	3461.36
	SPATA31 subfamily G member 1(SPATA31G1)	-5.22	1.78 E-07	-9.57	1.83
Educational attainment	DAPK1 intronic transcript 1(DAPK1-IT1)	-6.38	1.71 E-10	-0.10	0.02
	chromosome 16 open reading frame 96(C16orf96)	6.20	5.79 E-10	0.14	0.02
	transmembrane protein with EGF like and two follistatin like domains 2(TMEFF2)	-5.69	1.217 E-08	-0.12	0.02
	calcium homeostasis modulator 1(CALHM1)	-5.61	2.04 E-08	-0.06	0.01
	H1.10 linker histone(H1-10)	5.30	1.17 E-07	0.25	0.05
Uninsurance Rate	metallo-beta-lactamase domain containing 2(MBLAC2)	-5.93	3.11 E-09	-8.00	1.35
	syntaxin 2(STX2)	5.74	9.35 E-09	4.98	0.87
	cyclin dependent kinase 5 regulatory subunit 1(CDK5R1)	5.43	5.68 E-08	6.86	1.26
	heat shock protein 90 alpha family class B member 7, pseudogene(HSP90AB7P)	5.41	6.43 E-08	8.31	1.54
	junction mediating and regulatory protein, p53 cofactor(JMY)	-5.34	9.55 E-08	-10.61	1.99
	leishmanolysin like peptidase(LMLN)	-5.16	2.42 E-07	-6.64	1.29
	ADP ribosylation factor GTPase activating protein 1(ARFGAP1)	5.13	2.90 E-07	8.02	1.56
	Most strongly DEGs shown. Educational attainment = % of census block that has graduated from high school Uninsurance rate = % CB without health insurance Poverty= % of CB living below federal poverty level				
	All models controlling for patient age, gender, self reported race, bmi, and smoking, p value calculated with two way t test				

Title: Social Risk Factors and Receipt of Cancer Prevention Care in Community Health Center Patients

Authors:
Mateo Banegas[1], Jean O'Malley[2], Laura Gottlieb[3], Nathalie Huguet[4], Miguel Marino[4], Jorge Kaufmann[4], Rachel Gold[2,5] (presenting author)

[1]University of California, San Diego, [2]OCHIN Inc., [3]University of California, San Francisco, [4]Oregon Health & Science University, [5]Kaiser Permanente Center for Health Research

Abstract:
Background: Social risks (individual-level adverse social determinants of health) can pose barriers to receipt of cancer screening; this drives cancer disparities. To improve cancer screening equity requires understanding specific social risks' associations with different cancer screening processes.

Methods: Electronic health record data were extracted from n=458,552 adult patients with documented social risk screening results and an ambulatory visit at one of 186 community clinics (across 13 states) during 07/2016-02/2020. Outcomes of interest were associations between reported food, housing, or transportation insecurity and: 1) Proportion of study period in which patients were up to date on cervical (CVC), colorectal (CRC), and/or breast cancer (BC) screening; 2) Among patients due for a given screening, likelihood of receiving a relevant screening order; 3) Among those receiving an order, likelihood of order completion.

Findings: Patients reporting social risks were less likely to be up to date on CVC, CRC, or BC screening at baseline, and in most cases spent fewer study months up to date on these screenings. Receipt of screening orders was less likely for food insecure patients compared to those who were food secure. Completion of BC screening orders did not differ by social risk status. Order completion for CVC and CRC screenings was lower among food insecure than food secure patients. No clear relationship was seen between housing instability or transportation insecurity and cancer screening order receipt or completion.

Patients with social risks are less likely to be up-to-date with cancer screening than those without such risks. Different social risks influence whether patients receive and / or complete screening orders for different cancers. Findings advance D&I science by providing evidence that strategies intended to advance equitable adoption of these preventive care elements should consider the diverse pathways through which social risks create barriers to receipt of cancer screenings.

Title: Exploring the Mediating Effects of BMI on the Association between Social Deprivation and Neoadjuvant Chemotherapy Response in Pancreatic Cancer Patients

Authors:
Ming S. Lee[1] (presenting author), Mary P. Martos[2], Iago de Castro Silva[2], Anna Bianchi[2], Nilesh U Deshpand[2], Prateek Sharma[2,3], Siddharth Mehra[2], Vanessa Tonin Garrido[2], Shannon Jacqueline Saigh[1], Jonathan England[4], Peter Joel Hosein[1,5], Deukwoo Kwon[6], Nipun B Merchant[1,7], Jashodeep Datta[7]

[1]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine; [2]Department of Surgery, University of Miami Miller School of Medicine; [3]Department of Surgery, University of Nebraska Medical Center; [4]Department of Pathology, University of Miami; [5]Department of Medicine, University of Miami; [6]Department of Public Health Sciences, University of Texas Health Science Center at Houston; [7]Division of Surgical Oncology, Dewitt Daughtry Department of Surgery, University of Miami Miller School of Medicine

Abstract:
Background: Studies in public health have established that the social deprivation level of a neighborhood is associated with its obesity rate, which is a known risk factor for many types of cancer, including pancreatic cancer. It has also been reported that breast cancer patients with higher body mass indices (BMI) are more likely to have poor or no response from chemotherapy. This study aims to establish the connection between social deprivation and chemo responses by analyzing neighborhood social deprivation levels, BMIs, and neoadjuvant chemotherapy (NAC) responses in a group of pancreatic cancer patients.

Methods: A group of patients (n=119) with localized pancreatic ductal adenocarcinoma who received NAC with either mFOLFIRINOX, gemcitabine/abraxane, or both and underwent pancreatectomy between July 2015 and October 2022 at a tertiary academic center were enrolled in this study. Area Deprivation Index (ADI), based on socioeconomic data from US Census, for all Census block groups in the study area were obtained from the Center for Health Disparities Research of the University of Wisconsin. Residential addresses of the patients were geocoded to identify the associated ADIs. Contingency tables were used to explore the relationships among ADI, BMI, and chemo response.

Results: ADI was found to be negatively associated with neoadjuvant chemotherapy response in the patients, with higher rates of non-response in patients from neighborhoods of higher deprivation levels (e.g., lower income). Patients from areas with higher levels of deprivation tend to have higher BMIs, which are associated with higher rates of non-response for NAC. In addition, patients who were not responding to NAC have higher average neutrophil-to-lymphocyte ratios prior to surgery than those responded.

Conclusions: Results of this study suggest that social deprivation can negatively impact chemotherapy response, and BMI is a mediating biological factor between social deprivation and treatment outcomes in pancreatic cancer patients.

Title: Exploring Social Determinants of Health as Risk Factors for Cancer Treatment-Related Lymphedema

Authors:
Nicole L. Stout[1,2,3] (presenting author), Timothy Dotson[4], Sijin Wen[2,3,4], Morgan Denney[4], McKinzey Dierkes[4] (presenting author), Brian Witrick[4,5]

[1]Department of Cancer Prevention and Control, West Virginia University, Morgantown, WV, [2]Department of Public Health, West Virginia University, Morgantown, WV, [3]West Virginia University Cancer Institute, Morgantown, WV, [4]West Virginia Clinical and Translational Science Institute, Morgantown, WV, [5]Clemson University, Clemson, SC

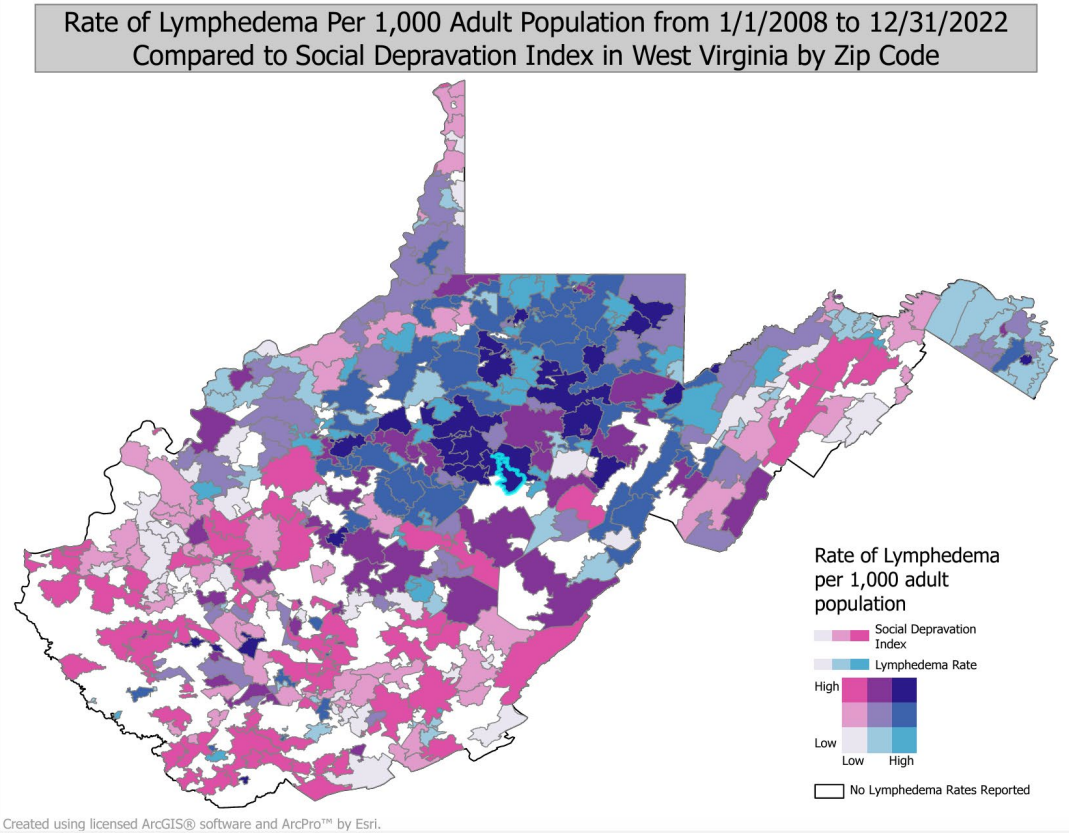
Abstract:
Background: There is a need to understand how social determinants of health influence the severity of cancer treatment related side effects, such as cancer treatment-related lymphedema (LE).[1] Risk factors for LE have been attributed to cancer treatment (removing lymph nodes/irradiating tissue) and comorbidity (vascular conditions/obesity). Emerging research suggests these risk factors are not independent, but interrelated factors that co-occur with other disease conditions to influence LE onset.[1] Considering the influence of social, behavioral, and environmental factors on cancer-related health outcomes,[3] we hypothesize that interrelationships exist between disease and social determinants and influence risk for LE. This exploratory analysis sought to identify the geographic relationship between social factors and LE.

Methods: Using retrospective EHR data 5500 patients from a single medical center in West Virginia were identified with a history of cancer and an ICD-10 code for LE. Patient zip code was mapped to the Social Depravation Index (SDI), a zip code tabulation area composite score of seven demographic factors that reflect local social determinants.[4] We created a bivariate choropleth map to explore the relationship between the population rate of LE (per 1000 adults) in a geographic zip code and SDI. Tertials for SDI and lymphedema rate were identified and mapped for comparison.

Results: Mapping rates of lymphedema/1000 adults in the population alongside SDI demonstrated that high rates of LE and high SDI co-occurred (**Figure 1**). Analysis is ongoing to understand between zip code comparisons and to examine SDI factors that drive LE risk using a non-LE control group. Preliminary results will be presented.

Conclusions: This map can help inform further investigation regarding resources allocation through policy and targeted interventions These findings suggest that future research should explore epigenetic changes related to social factors and their association with medical and comorbidity risk factors for LE.

Figure 1. Rate of Co-occurrence of Cancer-Related Lymphedema and Social Depravation



References:

1. Rochlin, D. H., Barrio, A. V., McLaughlin, S., et al. (2023). Feasibility and Clinical Utility of Prediction Models for Breast Cancer-Related Lymphedema Incorporating Racial Differences in Disease Incidence. JAMA Surg, 158(9), 954-964. https://doi.org/10.1001/jamasurg.2023.2414
2. Rockson SG, Zhou X, Zhao L, et al. Exploring disease interrelationships in patients with lymphatic disorders: A single center retrospective experience. Clinical and translational medicine. 2022;12(4):e760.
3. Afshar, N., English, D. R., & Milne, R. L. (2021). Factors Explaining Socio-Economic Inequalities in Cancer Survival: A Systematic Review. Cancer Control, 28, 10732748211011956. https://doi.org/10.1177/10732748211011956
4. Social deprivation index (SDI). Robert Graham Center - Policy Studies in Family Medicine & Primary Care. (2018, November 5). Retrieved November 2023 from https://www.grahamcenter.org/rgc/maps-data-tools/sdi/social-deprivation-index.html.

Title: A Multidisciplinary Approach to Explore the Intersection of Biology with Social Determinates of Health in the Development of Pain in Survivors of Head and Neck Cancer

Authors:
Monica A. Wagner[1,5] (presenting author), Fredrick R. Schumacher[2,5], Cheryl Cameron[2], Mark J. Cameron[2,5], Susan R. Mazanec[1,4,5], Yvette P. Conley[3], and Quintin Pan[2,4,5]

[1]Case Western Reserve University Frances Payne Bolton School of Nursing, [2]Case Western Reserve University School of Medicine, [3]University of Pittsburgh School of Nursing, [4]University Hospitals Seidman Cancer Center, [5]Case Comprehensive Cancer Center

Abstract:
Up to 85% of head and neck cancer (HNC) survivors report pain at diagnosis. Pretreatment pain is an independent predictor of survival in newly diagnosed HNC and is associated with recurrence within the first year. Currently, opioids are mainstay for pain relief in this population. Yet, this analgesic strategy relies on clinician interpretation of patient reported pain and overlooks social and biological factors that may influence pain perception, opioid tolerance, and risk of dependence. Research exploring the biological and social factors of HNC-related pain is needed to better stratify and provide pain management. This study explores drivers of HNC-related pain in the context of social/demographic, and biological (transcriptome, methylome) factors (biomarkers) prior to definitive treatment in newly diagnosed oral cavity or oropharyngeal patients (n=15). Using the Brief Pain Inventory-Worst Pain item, 10 participants self-reported any pain, while 7 reported a score of ≥4 (moderate to severe pain). Six total participants had evidence of perineural invasion (PNI). The area deprivation index (ADI) of those reporting pain ≥4 was 74.0 ± 5.3 while those reporting no pain had an ADI of 64.2 ± 12.2. Those reporting pain ≥4 also lived twice the distance from where they received treatment than those who reported no pain (52.3 ± 11.2 vs. 22.6 ± 5.6 mi). A systems biology approach will be employed to correlate transcriptome and methylome data with PNI status and pretreatment pain scores. Our interdisciplinary approach to understanding HNC-related pain will provide insight for clinicians and researchers on the intersection of biology and social determinants. This information can be leveraged to construct predictive risk models, potential therapeutic targets, and strategies to ensure that HNC survivors receive precision pain management to enable more pain free days, lessen morbidity and disability, and substantially improve the quality of their lives.

Title: Social genomics as a framework for understanding health disparities among adolescent and young adult cancer survivors.

Authors:
Brad Zebrack[1] (presenting author), Steve Cole[2], John M. Salsman[3], Lynne Wagner[4], Fenghai Duan[5], Ilana Gareen[5], Susan K. Parsons[6], Andrew Evens[7], Christabel Cheung[8], Lauren Lux[4], Lauren V. Ghazal[9], Brad Kahl[10], Pinki Prasad[11], Shira Dinner[12]

[1]University of Michigan, [2]University of California, Los Angeles, [3]Wake Forest University, [4]University of North Carolina, [5]Brown University, [6]Tufts University, [7]Rutgers University, [8]University of Maryland, [9]Rochester University, [10]ECOG-ACRIN Lymphoma Committee Chair, [11]ECOG-ACRIN Community Cancer Center Chair, [12]Nortwestern University

Abstract:
Background/Purpose: AYA cancer survivors (aged 18-39 years at diagnosis) experience unique psychosocial stressors and life disruptions having ramifications for their health, mental health, and quality of life (QOL). Health outcomes, and disparities in outcomes, may be partially a function of social determinants of health, including socioeconomic gradients, exposures to childhood traumas or adversity, and accumulated experiences of discrimination. Yet, little is known about if and how these social environmental conditions influence morbidity, mortality, and QOL among AYAs. The purpose of the research proposed here is to identify and define functional genomic pathways through which current and past psychosocial and social environmental risk and resilience factors influence gene regulation and subsequent health outcomes in AYAs, thus contributing to a greater understanding of health disparities in post-treatment survivorship.

Methodology: In collaboration with the Eastern Cooperative Oncology Group-American College of Radiology Imaging Network (ECOG-ACRIN) and the NCI Community Oncology Research Program (NCORP), we have initiated a 5-year longitudinal prospective cohort study of 2000 Hodgkin and non-Hodgkin lymphoma survivors recruited within one year following completion of treatment. Using a "social genomics" framework, which hypothesizes a biological basis for psychological and social influences on outcomes, we aim to identify neural and molecular pathways (i.e., CTRA gene regulation by the sympathetic nervous system) through which psychological and social factors mechanistically influence disease development and progression. Using Patient Reported Outcomes measures and blood assays, we will evaluate (1) the extent to which biological, psychological, and social indicators are associated with and potentially predict mortality, morbidity, and QOL in AYA cancer survivors within two years following completion of therapy; and (2) variations by race/ethnicity, sexual orientation, and gender identity.

Results: Results will inform the conceptualization and development of targeted medical and supportive care interventions that reduce risks for morbidity and mortality and improve QUALITY of life for AYAs.