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Project Requirements and Description

Requirements to submit AOI (all answers must be "yes" to proceed)

A comprehensive review of previously published data has been completed	Yes
The specific aims are clear and focused	Yes
The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator.	Yes
The investigator agrees to develop an initial draft of the concept proposal within 6 weeks of approval of the AOI and to finalize the concept proposal within 6 months	Yes

Project Title Genetic Liability and Risk Prediction of Psychiatric Outcomes in Childhood Cancer Survivors

Planned research population (eligibility criteria)

All participants (original and expansion cohort) who have BSI-18 data from baseline assessment and at least two additional follow-ups and have genome-wide data.

Proposed specific aims

Aim 1: To identify common genetic variants associated with baseline measures of global psychological distress and specific symptom dimensions (i.e. anxiety, depression, somatization) using CCSS as the discovery. We will first conduct genome-wide association studies (GWASs) separated by genetic ancestry, and subsequently, we will meta-analyze across ancestries to identify trans-ancestry associations. Genome- wide significant associations from ancestry-specific or trans-ancestry analyses will be evaluated in the SJLIFE cohort.

Aim 2: Conduct longitudinal GWAS (longGWAS or trajGWAS) to determine if there are specific common variants associated with different longitudinal patterns of global psychological distress and specific symptom dimensions (i.e. increased distress/symptoms, decreased distress/symptoms, no change in distress/symptoms) with CCSS as the discovery sample and SJLIFE as the replication sample

Aim 3: Identify functional consequences and downstream pathways of associated variants using functional annotation and estimate the proportion of variation explained by common variants using GWAS summary statistics from Aims 1 and 2 and compare results from childhood cancer survivors to findings from the general population.

Aim 4: Develop risk prediction models in CCSS for psychiatric outcomes in childhood cancer survivors and validate it in SJLIFE.

Will the project require non-CCSS funding to complete? No

If yes, what would be the anticipated source(s) and timeline(s) for securing funding?

Does this project require contact of CCSS study subjects for:

Additional self-reported information	No
Biological samples	No
Medical record data	No

If yes to any of the above, please briefly describe.

What CCSS Working Group(s) would likely be involved? (Select all that apply)

	Primary	Secondary
Second Malignancy		
Chronic Disease		
Psychology/Neuropsychology		✓
Genetics	✓	
Cancer Control		
Epidemiology/Biostatistics		✓

Outcomes or Correlative Factors

	Primary	Secondary	Correlative Factors
Late Mortality			
Second Malignancy			

Health Behaviors

	Primary	Secondary	Correlative Factors
Tobacco			✓
Alcohol			✓
Physical Activity			
Medical Screening			
Other			

If other, please specify

Psychosocial

	Primary	Secondary	Correlative Factors
Insurance			✓
Marriage			✓
Education			✓
Employment			✓
Other			

If other, please specify

Medical Conditions

	Primary	Secondary	Correlative Factors
Hearing/Vision/Speech			
Hormonal Systems			
Heart and Vascular			
Respiratory			
Digestive			
Surgical Procedures			

	Primary	Secondary	Correlative Factors
Brain and Nervous System			
Other			

If other, please specify

Medications

Describe medications

anti-depressants and anxiolytics

Psychologic/Quality of Life

	Primary	Secondary	Correlative Factors
BSI-18	✓		
SF-36			
CCSS-NCQ			
PTS			
PTG			
Other			

If other, please specify

Other

	Primary	Secondary	Correlative Factors
Pregnancy and Offspring			
Family History			✓
Chronic Conditions (CTCAE v3)			✓
Health Status			

Demographic

	Primary	Secondary	Correlative Factors
Age			✓
Race			✓
Sex			✓
Other			

If other, please specify

Cancer Treatment

	Correlative Factors
Chemotherapy	✓
Radiation Therapy	✓
Surgery	✓

Anticipated Sources of Statistical Support

CCSS Statistical Center	No
Local Institutional Statistician	Yes

If local, please provide the name(s) and contact information of the statistician(s) to be involved.

Will this project utilize CCSS biologic samples? No

If yes, which of the following?

If other, please explain

Other General Comments

Agree

I agree to share this information with St. Jude

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