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Project Requirements and Description

Requirements to submit AOI

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 Hematopoietic Loss of X or Y Chromosome in Childhood Cancer Survivors

Planned research population (eligibility criteria)

Participants with whole exome sequencing or whole genome sequencing performed from blood samples after cancer treatment.

Proposed specific aims

Age-related morbidity and mortality is promoted by genomic instability, including hematopoietic mosaic loss of the X or Y chromosome. This phenomenon is acquired in the elderly population with age and results in some blood cells with an X0 genotype that contribute to several age-related pathologies. Other genotoxic stressors (smoking, pesticides) are known to promote the accumulation of X or Y chromosome loss, but the effects of cancer treatments on X or Y chromosome loss have not been studied. We hypothesize that hematopoietic mosaic loss of X or Y chromosome will be observed in childhood cancer survivors previously treated with chemotherapy or radiation. To this end, we propose the following specific aims:
1) Determine the extent of X chromosome loss in female participants and Y chromosome loss in male participants using mosaic chromosomal abnormality analyses of whole genome sequencing or whole exome sequencing data acquired from blood samples.

2) Correlate loss of X or Y chromosome with treatment protocol to determine whether radiation or specific chemotherapy administrations differentially affect sex chromosome stability.
3) Correlate loss of X or Y chromosome with clinical outcomes to determine whether greater loss of X or Y chromosome increases risk of other medical conditions in childhood cancer survivors.
Through these experimental aims, we intend to elucidate whether mosaic loss of X or Y chromosome in blood could be a consideration for health outcomes of childhood cancer survivors.

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	✓		
Brain and Nervous System	✓		

If other, please specify

Medications

Describe medications

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	Yes
Local Institutional Statistician	No

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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