**Section: Contact Information**

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**Section: Project Requirements and Description**

**Group: Requirements to submit AOI**

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: Clinical and Genetic Profiling of Cataract Risk among Long-Term Childhood Cancer Survivors  
Planned research population (eligibility criteria) :  

**Study participants:**

The Discovery cohort will include participants from the Childhood Cancer Survivor Study (CCSS) who i) have survived at least 5 years after diagnosis of leukemia, CNS malignancy, Hodgkin lymphoma, non-Hodgkin lymphoma, Wilms tumor, neuroblastoma, soft tissue sarcoma, or a bone tumor; ii) available genotype data; iii) available phenotype data on study outcome.  
The Replication cohort will include participants from the Blood or Marrow Transplant Survivor Study (BMTSS) who i) received BMT following a cancer diagnosis between 1974 and 2014 and survived ≥2y after BMT; ii) available DNA samples; iii) available phenotype data on study outcome.  

**Outcome:**

Self-reported diagnosis of cataract and receipt of cataract surgery will be extracted from the longitudinal CCSS cohort for patients completing the Expansion Baseline Survey, Follow-Up 4 (2007) and Follow-Up 5 (2014) for Discovery; and from the BMTSS questionnaire for Replication. The self-reported outcome is a report of being diagnosed with cataract by a physician and/or receiving cataract surgery.  

**Proposed specific aims:**

Aim 1: Identify single nucleotide polymorphisms (SNPs) associated with cataract risk among long-term survivors of childhood cancer.  
Aim 1.1: Identify individual SNP associations using the CCSS cohort (Discovery)  
Aim 1.2: Externally replicate the significant SNP associations in an independent cohort of BMTSS survivors (Replication).
Ho: Individual SNPs are associated with increased cataract risk among long-term childhood cancer survivors.

Aim 2: Develop a risk prediction model that integrates clinical and genetic factors to identify cancer survivors at high risk for cataract.

Aim 1.1: Develop a risk prediction model using the CCSS cohort (Discovery)

Aim 1.2: Externally validate the model in an independent cohort of cancer survivors treated with BMT (Replication).

Ho: A combined clinical and genetic model applied to childhood cancer survivors will have a discriminative power as assessed by a C-statistic ≥0.65 to identify individuals at high risk of cataract.

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?:

**Group: 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: 

**Group: What CCSS Working Group(s) would likely be involved? (Check all that apply)**

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

**Section: Outcomes or Correlative Factors**

Late mortality: 
Second Malignancy: 

**Group: Health Behaviors**

Tobacco: Correlative Factors
Alcohol: Correlative Factors
Physical activity: 
Medical screening: Correlative Factors
Other: 
If other, please specify: 

**Group: Psychosocial**

Insurance: 
Marriage: 
Education: 
Employment: 
Other: 
If other, please specify: 

**Group: Medical Conditions**
Hearing/Vision/Speech: **Primary**

Hormonal systems:
Heart and vascular:
Respiratory:
Digestive:
Surgical procedures:
Brain and nervous system:
Other:
If other, please specify:

**Group: Medications**
Describe medications:

**Group: Psychologic/Quality of Life**
BSI-18:
SF-36:
CCSS-NCQ:
PTS:
PTG:
Other:
If other, please specify:

**Group: Other**
Pregnancy and offspring:
Family history:
Chronic conditions (CTCAE v3): **Correlative Factors**
Health status:

**Group: Demographic**
Age: **Correlative Factors**
Race: **Correlative Factors**
Sex: **Correlative Factors**
Other:
If other, please specify:

**Group: Cancer treatment**
Chemotherapy: **Correlative Factors**
Radiation therapy: **Correlative Factors**
Surgery:

**Section: Anticipated Sources of Statistical Support**
CCSS Statistical Center: **Yes**
Local institutional statistician: **Yes**
If local, please provide the name(s) and contact information of the statistician(s) to be involved:
Joshua Richman, MD PhD and Lucy Zhou, MS
Institute for Cancer Outcomes and Survivorship
Birmingham, AL 35233
(205) 638-2128 or 638-2120
(205) 638-2121 fax
Will this project utilize CCSS biologic samples? : No
If yes, which of the following? :
If other, please explain :

**Section: Other General Comments**

Other General Comments :
I agree to share this information with St. Jude : Yes