

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 : **Germline Genomics to Identify Genetic Variants that Predispose Childhood Cancer Survivors Diagnosed During 1987-1999 to the Development of Subsequent Neoplasms**

Planned research population (eligibility criteria) :

Survivors diagnosed with first primary childhood cancer during 1987-1999 with available DNA

Proposed specific aims :

The Division of Cancer Epidemiology and Genetics, National Cancer Institute (DCEG/NCI) has collaborated with CCSS to conduct genome-wide single nucleotide polymorphism (SNP) genotyping and whole exome sequencing on over 5000 CCSS participants originally diagnosed with childhood cancer during 1970-1986. The specific aims of that ongoing project are to:

- 1) identify genetic variants associated with the development of subsequent neoplasms among childhood cancer survivors, considering variants that are dependent or independent of treatment exposures.**
- 2) identify genetic variants associated with the risk of childhood cancer.**
- 3) develop a resource of germline genomics data that can be used to evaluate genetic susceptibility to other late adverse outcomes among childhood cancer survivors.**

We now propose to expand the genomics data in CCSS to include recently recruited study participants who were originally diagnosed during 1987-1999. The objective of this proposal is to expand the sample size for ongoing analyses, leveraging the same high-throughput Cancer Genomics Research Laboratory (CGR) within DCEG combined with the recent expansion of the CCSS cohort to include more recently diagnosed survivors, with collection of treatment, follow-up, and outcome data that are comparable to the original cohort. To date, CCSS has collected Oragene samples for over 4500 individuals from the expansion cohort, with complete follow-up through 2015. Proposed genomics analyses on the expansion cohort include: 1) SNP genotyping using the Illumina Infinium Global Screening Array (GSA), which includes 660,000 markers that serve as a strong backbone for subsequent imputation, and 2) whole exome sequencing. We are seeking Intramural NIH funds over the next several years to support the sample handling, laboratory work, and bioinformatics, as well as statistical analyses for Aims 1-2 and posting of data to facilitate data sharing for Aim 3.

The long-term goals of these studies are to further advance understanding of genetic susceptibility to subsequent neoplasms and other adverse events in childhood cancer survivors, elucidate mechanisms of radiation- and chemotherapy-induced cancer and other diseases, and provide insight into susceptibility to childhood cancer. Ultimately, the study results have the potential to directly impact clinical decision-making in terms of treatment and long-term follow-up of childhood cancer survivors.

Will the project require non-CCSS funding to complete? : **Yes**

If yes, what would be the anticipated source(s) and timeline(s) for securing funding? : **We are seeking Intramural NIH funds, with anticipation of availability of funds over two years.**

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 : **Secondary**

Chronic Disease :

Psychology / Neuropsychology :

Genetics : **Primary**

Cancer Control :

Epidemiology / Biostatistics : **Secondary**

Section: Outcomes or Correlative Factors

Late mortality : **Correlative Factors**

Second Malignancy : **Primary**

Group: Health Behaviors

Tobacco : **Correlative Factors**

Alcohol : **Correlative Factors**

Physical activity : **Correlative Factors**

Medical screening :

Other :

If other, please specify :

Group: Psychosocial

Insurance :

Marriage :

Education :

Employment :

Other :

If other, please specify :

Group: Medical Conditions

Hearing/Vision/Speech :

Hormonal systems : **Correlative Factors**

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 : **Correlative Factors**

Family history : **Correlative Factors**

Chronic conditions (CTCAE v3) :

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 : **Correlative Factors**

Section: Anticipated Sources of Statistical Support

CCSS Statistical Center :

Local institutional statistician : **Yes**

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

Joshua Sampson (sampsonjn@mail.nih.gov) - Division of Cancer Epidemiology and Genetics, National Cancer Institute

Will this project utilize CCSS biologic samples? : **Yes**

If yes, which of the following? : **Buccal cell DNA, Peripheral blood**

If other, please explain :

Section: Other General Comments

Other General Comments :