

Section: Contact Information

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Institution : **National Cancer Institute, Division of Cancer Epidemiology and Genetics**

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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 : **Genetic Susceptibility to Certain Subsequent Neoplasms after Radiotherapy for Childhood Cancer**

Planned research population (eligibility criteria) :

CCSS expansion cohort members with WGS data

Proposed specific aims :

To leverage the whole genome sequencing data in the CCSS Expansion Cohort to augment ongoing analyses in the CCSS Original Cohort to identify rare coding variants and genome-wide common variants that are associated with risk for developing subsequent neoplasms in three key categories:

- 1. Radiation-related subsequent neoplasms (as a group, no primary discovery in a specific type)**
- 2. Breast cancer**
- 3. Thyroid cancer**

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? :

The analysis will be fully supported by the Intramural Research Program of the National Cancer Institute.

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 :

Section: Outcomes or Correlative Factors

Late mortality :

Second Malignancy : **Primary**

Group: Health Behaviors

Tobacco :

Alcohol :

Physical activity :

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 :

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) :

Health status :

Group: Demographic

Age :

Race :

Sex :

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 :

Local institutional statistician : **Yes**

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

Joshua Sampson, PhD

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 :

1. Analyses will consider all childhood cancer survivors as well as stratifying the population by radiation dose to the site of the subsequent neoplasm. Radiation dose will be estimated using body-region dosimetry. Cytotoxic chemotherapy exposure will be adjusted for in the models.

2. Pending discussions with and agreement from all involved PIs, data may be combined with additional studies to maximize power for discovery and evaluate consistency of results in independent populations, e.g., an NCI collaboration with a case-control study of breast cancer after Hodgkin lymphoma, an NCI-led study of breast cancer in patients with Li Fraumeni Syndrome, and an NCI-led study of thyroid cancer after the Chernobyl accident.

I agree to share this information with St. Jude : **Yes**