

## **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 : **Factors Contributing to Survival Following Second Malignant Neoplasms Diagnosed in Long-term Survivors of Childhood Cancer**

Planned research population (eligibility criteria) :

**Long-term (>5 year) survivors of childhood cancer diagnosed with a second malignant neoplasm**

Proposed specific aims :

**1. Evaluate the impact of comorbid chronic health conditions on all-cause and cancer-specific mortality following a diagnosis of a second malignant neoplasm among long-term survivors of childhood cancer.**

**Hypothesis: Prevalent chronic health conditions (any grade 3-5 condition, multiple grade 3-5 conditions, and specific grade 3-5 conditions [e.g., cardiac, endocrine, pulmonary]) will adversely impact survival among long-term survivors of childhood cancer diagnosed with a second malignant neoplasm.**

**2. Determine the association between frailty phenotypes and all-cause and cancer-specific mortality following a diagnosis of a second malignant neoplasm among long-term survivors of childhood cancer.**

**Hypothesis: Compared to non-frail childhood cancer survivors, frail and pre-frail survivors will experience poorer overall and cancer-specific survival following a second malignant neoplasm.**

**3. Identify childhood cancer therapeutic exposures associated with all-cause and cancer-specific mortality following a diagnosis of a second malignant neoplasm among long-**

term survivors of childhood cancer.

**Hypothesis: Specific therapeutic exposures during childhood (e.g., radiation, alkylating agents, platinum agents, anthracycline) will be associated with a poorer prognosis among survivors diagnosed with second malignant neoplasms.**

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 : **Secondary**

Chronic Disease : **Secondary**

Psychology / Neuropsychology : **Secondary**

Genetics :

Cancer Control : **Secondary**

Epidemiology / Biostatistics : **Primary**

**Section: Outcomes or Correlative Factors**

Late mortality : **Primary**

Second Malignancy : **Correlative Factors**

**Group: Health Behaviors**

Tobacco :

Alcohol :

Physical activity : **Correlative Factors**

Medical screening :

Other :

If other, please specify :

**Group: Psychosocial**

Insurance : **Correlative Factors**

Marriage : **Correlative Factors**

Education : **Correlative Factors**

Employment : **Correlative Factors**

Other :

If other, please specify :

**Group: Medical Conditions**

Hearing/Vision/Speech :

Hormonal systems : **Correlative Factors**

Heart and vascular : **Correlative Factors**

Respiratory : **Correlative Factors**

Digestive : **Correlative Factors**

Surgical procedures : **Correlative Factors**

Brain and nervous system : **Correlative Factors**

Other :

If other, please specify :

***Group: Medications***

Describe medications :

***Group: Psychologic/Quality of Life***

BSI-18 :

SF-36 : **Correlative Factors**

CCSS-NCQ :

PTS :

PTG :

Other :

If other, please specify :

***Group: Other***

Pregnancy and offspring :

Family history :

Chronic conditions (CTCAE v3) : **Correlative Factors**

Health status : **Correlative Factors**

***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. :

**This project will be conducted in collaboration with Dr. Kiri Ness. Analyses will be conducted under her supervision at St. Jude Children's Research Hospital.**

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 :

**Curative childhood cancer therapy places survivors at increased risk of chronic health conditions, frailty, and second primary malignancies (SPMs). Leveraging data from the**

Surveillance, Epidemiology, and End Results (SEER) program, we recently compared survival in childhood cancer survivors who developed second primary malignancies (SPMs) to individuals with comparable first primary malignancies (FPMs). Compared with individuals with FPMs, childhood cancer survivors with a similar SPMs experienced poorer OS (HR=1.86, 95% CI: 1.72-2.02) after accounting for age, sex, race, and decade of diagnosis. A history of childhood cancer remained a poor prognostic factor for all specific cancers evaluated, including: breast (HR=2.07, 95% CI: 1.63-2.62), thyroid (HR=3.59, 95% CI: 2.08-6.19), acute myeloid leukemia (HR=2.38, 95% CI:1.87-3.05), brain (HR=2.09, 95% CI:1.72-2.55), melanoma (HR=2.57, 95% CI: 1.55-4.27), bone (HR=1.88, 95% CI:1.37-2.57), and soft tissue sarcoma (HR=2.44, 95% CI: 1.78-3.33). The objective of this CCSS proposal is to evaluate whether chronic health conditions, frailty, or specific childhood therapeutic exposures are associated with inferior outcomes among childhood cancer survivors diagnosed with SPMs.

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