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: Robust Genetic Predictors of Secondary Cancer Risks

Planned research population (eligibility criteria): 1. All CCSS subjects for whom lymphoblastoid cell lines are available

Proposed specific aims:
1. To identify the prevalence of germline defects in the double strand break repair and mismatch repair pathways in survivors of childhood cancer by primary cancer type using flow variant assays (FVAs).

2. To identify the prevalence of DNA repair defects in SN and adjacent normal tissues in survivors of childhood cancer by cancer type and radiotherapy exposure using whole genome sequencing (WGS).

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?: NIH R01 support with proposal submission June, 2020.

Group: Does this project require contact of CCSS study subjects for:

Additional self-reported information: No
Biological samples: Yes
Medical record data: Yes
If yes to any of the above, please briefly describe.: All lymphoblastoid cell lines for FVA testing. Additional frozen PBMCs for LCL transformation and FVA testing. Tumor blocks for dissection, DNA extraction and whole genome sequencing
Prior genetic testing results

Secondary malignancies

**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: Secondary
Second Malignancy: Primary, Correlative Factors

**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: Primary
Chronic conditions (CTCAE v3):
Health status:

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

**Group: Cancer treatment**
Chemotherapy:
Radiation therapy:
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.:
Yongzhao Shao, Ph.D. - yongzhao.shao@nyulmc.org

Lindsay Mortin, Ph.D. - mortonli@mail.nih.gov
Will this project utilize CCSS biologic samples?: Yes
If yes, which of the following?:
Lymphoblastoid cell lines, PBMCs, tissue blocks
If other, please explain:

**Section: Other General Comments**
Other General Comments:
Flow variant assays were developed in my laboratory to identify germline defects in genetic pathways. We have developed assays for the DSB repair and MMR pathways and are applying these for predicting adult cancer risks. Sequencing of tumors and radiation exposed normal tissue represents an alternative method for identifying defects in DNA repair pathways.

We will develop a bidirectional workflow with Lindsay Morton to share data and analyses.
I agree to share this information with St. Jude: Yes