

## **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 : **Return of Genomic Results to Research Participants: A Childhood Cancer Survivor Study Ancillary Study**

Planned research population (eligibility criteria) :

**4086 CCSS participants whose biologic samples are being utilized for whole exome sequencing. Excludes St. Jude Lifetime Cohort Participants, Canadians, deceased participants and those no longer participating in the CCSS.**

Proposed specific aims :

**Next generation sequencing, including genome-wide association studies and whole-exome sequencing (WES) have great promise for improving human health and reducing cancer burden, propelling the rapidly expanding field of precision medicine. Large prospective cohort studies with banked DNA have increasingly utilized next generation sequencing (NGS) to evaluate the effects and interplay of genes, the environment and lifestyle. Concomitant with WES are incidental findings, many of which may be of significant importance to an individual's health. There is an emerging consensus that "actionable" incidental findings should be considered for return to research participants as they could be important to the health of research participants and their families. Additionally, current guidelines recommend that research participants' preferences for receipt of actionable research findings be honored. Despite these recommendations, there is limited data on the risks, benefits and utility of returning actionable**

individual research results (IRR), and no consensus on how to best communicate IRR, particularly in large, geographically diverse cohort studies, so that participants can make informed decisions about whether to receive them. Communication with a genetic counselor will not be feasible for many large research cohorts, and recent studies suggest that telephone delivery with a genetic provider is a reasonable option, but this approach still may not be scalable in large cohorts. Given that research results must still be clinically confirmed after receipt, providing an opportunity to consider receipt of IRR and providing results through a secure website (with the option to speak to a genetic counselor) provides a scalable alternative, which preliminary data suggest may be acceptable to patients.

The overall goal of the proposed research is to evaluate the short-term and longitudinal risks, benefits, utilities and costs of returning actionable individual genetic research results identified through WES to research participants by two remote methods: 1) by phone with a genetic provider; or 2) via a secure electronic web portal, with the option to speak with a genetic provider according to patient preferences. The Childhood Cancer Survivor Study is a North American cohort of over 30,000 childhood cancer survivors diagnosed with their primary cancer between 1970 and 1999. WES is planned on over 4000 participants for whom banked DNA is available to identify risk factors for second cancers among participants. Original consents to the CCSS stated that research results would not be returned. In this study, we will first contact all participants to provide them an opportunity to consider their preferences for receipt of individual research results and to opt-out of receipt of actionable results, if this is their preference. Building upon related work in the RESPECT study (R01CA190871:Bradbury), participants will be provided access to an education website which will review what results could be available and the risks, benefits and limitations of receiving IRR. We estimate that over 400 survivors will be identified to have one or more actionable genetic findings. Among those who have not opted out of receiving IRR, we propose to evaluate the short-term and longitudinal cognitive, affective and behavioral outcomes of sharing actionable genetic research results (which ultimately will need to be confirmed with clinical testing) via phone with a genetic provider as compared to return via an electronic web portal, with the option to speak with a genetic provider either before or after receipt of results. In both arms participants would require confirmation testing of their research finding before changing their medical management.

**Aim 1:** To evaluate the efficacy of disclosure by a secure electronic web portal with genetic provider support based on patient preferences to provide equal or improved short-term outcomes (knowledge, psychological distress, satisfaction with genetic services, behavioral intentions and costs) as compared to telephone disclosure with a genetic provide.

**Aim 2:** To evaluate the efficacy of disclosure by a secure electronic web portal

with genetic provider support based on patient preferences to provide equal or improved longitudinal outcomes (knowledge, psychological distress, satisfaction with genetic services, health and psychosocial behaviors) as compared to telephone disclosure with a genetic provide.

**Aim 3: To evaluate potential moderators, as suggested by Self-Regulation Theory of Health Behavior (genetic test, genetic test result, patient sociodemographics and preference for delivery modality) of: a) opting out of receipt of IRR and b) to the impact of disclosure by a secure electronic web portal with genetic provider support based on patient preferences on short term and longitudinal outcomes of receiving IRR.**

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 will be submitting to the NIH Societal and Ethical Issues in Research Study Section for the February 5, 2016 deadline.**

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

Additional self-reported information : **Yes**

Biological samples : **No**

Medical record data : **No**

If yes to any of the above, please briefly describe. :

**We will be contacting CCSS participants whose samples are undergoing whole exome sequencing to enable them to opt out of receiving actionable genetic findings and then we will randomizing those with identified actionable genetic findings to receipt of results via telephone with a genetic counselor versus website with the option to speak to a genetic counselor. The study will require a baseline survey and follow-up surveys.**

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

Second Malignancy :

Chronic Disease :

Psychology / Neuropsychology : Secondary

Genetics : **Secondary**

Cancer Control : **Primary**

Epidemiology / Biostatistics :

### **Section: Outcomes or Correlative Factors**

Late mortality :

Second Malignancy :

**Group: Health Behaviors**

Tobacco :

Alcohol :

Physical activity :

Medical screening : **Correlative Factors**

Other : **Correlative Factors**

If other, please specify : **Reported health care utilization**

***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 :

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 : **Correlative Factors**

SF-36 : **Correlative Factors**

CCSS-NCQ :

PTS :

PTG :

Other :

If other, please specify :

***Group: Other***

Pregnancy and offspring :

Family history : **Correlative Factors**

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. :

**Brian Egleston, MPP, PhD**

**Fox Chase Cancer Center**

[Brian.Egleston@fcc.edu](mailto:Brian.Egleston@fcc.edu)

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 :

**We are in the process of collecting pilot data through the St. Jude Lifetime Cohort.**