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 : **Validation of interactome-based biomarkers of inherited susceptibility to radiation-induced carcinogenesis.**

Planned research population (eligibility criteria) :

Individuals treated with radiotherapy for primary cancers other than leukemia or NHL who either did or did not develop radiation-associated secondary breast or thyroid cancers. Matched controls without secondary cancers would ideally come from age, sex, and race / ethnicity matched individuals with the same primary cancer and treatment as the person with the secondary cancer, and with a cancer-free follow up period longer than that of the person with the secondary cancer.

Proposed specific aims :

Prior to our proposed CCSS study, we will use frozen blood samples from a unique Israeli cohort that shows strong familial predisposition to radiation induced cancers and apply a cutting-edge interactome analysis approach to identify master regulators with altered function in individuals showing predisposition to radiation-induced cancer. The hypothesis to be tested using samples from the CCSS is that the same network dysregulation and master regulator functions underlying the susceptibility to radiation-induced cancer in the Israeli cohort will be broadly generalizable to radiation-associated second cancers occurring at other sites. We will test for the presence of the same

network signature in frozen blood samples from individuals who developed radiotherapy-associated second breast and thyroid cancer. This study can only be successful in a cohort where radiation treatment p roduces high relative risks for carcinogenesis, as the majority of cancers arising in irradiated adults are sporadic.

Specific Aim: Apply RNA-Seq and intractome analysis to CCSS samples from radiation-treated individuals who did or did not develop a second cancer, and compare the rank-ordered lists of disregulated master regulators to those from the Israeli cohort to test for the contribution of the same underlying genetic susceptibility to radiation-induced cancer to second cancer development in the CCSS cohort.

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? : **Application to NIH FOA PAR-13-081, due June 17, 2015. (Earliest start date April 2016)**

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 :
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. :
statistics: Shuang Wang sw2206@cumc.columbia.edu
informatics: Yishai Shimoni ys2559@cumc.columbia.edu
modeling: Igor Shuryak is144@cumc.columbia.edu

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

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

If other, please explain :

Section: Other General Comments

Other General Comments :