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 produces high relative risks for carcinogenesis, as the majority of cancers arising in irradiated adults are sporadic.

Specific Aim: Apply RNA-Seq and interactome analysis to CCSS samples from radiation-treated individuals who did or did not develop a second cancer, and compare the rank-ordered lists of deregulated 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@cums.columbia.edu
informatics: Yishai Shmoni ys2559@cums.columbia.edu
modeling: Igor Shuryak is144@cums.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: