

CCSS Application of Intent Submission

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Project Requirements and Description

Requirements to submit AOI:

	Yes	No
A comprehensive review of previously published data has been completed	✓	-
The specific aims are clear and focused	✓	-
The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator.	✓	-
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	✓	-

Project Title:

Epigenetic Approach in Understanding the Risk of Cardiometabolic Conditions

Planned research population:

2,885 survivors with pre-existing WGS/WES and new DNA methylation profiling data to be generated with stored blood samples.

Proposed specific aims:

Aim 1: Evaluate epigenetic factors (specifically, DNA methylation) as mediators of the association between cancer treatment exposures or health behaviors and risk of cardiometabolic conditions.

Aim 2: Evaluate epigenetic age as an independent predictor of cardiometabolic risk, while adjusting for genetic and epigenetic factors.

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

Does this project require contact of CCSS study subjects for:

	Yes	No
Additional self-reported information		✓
Biological samples	-	✓
Medical record data		✓

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

Cardiometabolic conditions including five modifiable CVD risk increasing conditions (abnormal glucose metabolism, obesity, hypertension, hypertriglyceridemia, and hypercholesterolemia) and two end-organ cardiac damage (cardiomyopathy and myocardial infarction).

What CCSS Working Group(s) would likely be involved?:

	Primary	Secondary
Second Malignancy	-	-
Chronic Disease	-	✓
Psychology/Neuropsychology	-	-
Genetics	✓	-
Cancer Control	-	-
Epidemiology/Biostatistics	-	-

Outcomes or Correlative Factors

Late Mortality and Second Malignancy: Not selected

Health Behaviors:

	Primary	Secondary	Correlative Factors
Tobacco	-	-	✓
Alcohol	-	-	✓
Physical Activity	-	-	✓
Medical Screening	-	-	✓
Other	-	-	-

If other, please specify:

Psychosocial: Not selected

If other, please specify:

Medical Conditions:

	Primary	Secondary	Correlative Factors
Hearing/Vision/Speech	-	-	-
Hormonal Systems	-	-	-
Heart and Vascular	✓	-	-
Respiratory	-	-	-
Digestive	-	-	-
Surgical Procedures	-	-	-
Brain and Nervous System	-	-	-
Other	-	-	-

If other, please specify:

Medications

Describe medications:

Psychologic/Quality of Life: Not selected

If other, please specify:

Other:

Demographic:

	Primary	Secondary	Correlative Factors
Age	-	-	✓
Race	-	-	✓
Sex	-	-	✓
Other	-	-	-

If other, please specify:

Cancer Treatment:

	Correlative Factors
Chemotherapy	✓
Radiation Therapy	✓
Surgery	-

Anticipated Sources of Statistical Support:

	Yes	No
CCSS Statistical Center	✓	-
Local Institutional Statistician	✓	-

If local, please provide the name(s) and contact information of the statistician(s) to be involved: Qian Dong, PhD email: Qian.Dong@stjude.org

Will this project utilize CCSS biologic samples?: Yes

If yes, which of the following?:

If other, please explain:

Other General Comments

General comments: I discussed with Dr. Armstrong about adding this set of CCSS data (new, pending on the CCSS Supplement funds) for replication in my R01 grant application where ~4000 survivors in SJLIFE with genetic/epigenetic data will be used for discovery to study the mechanisms of increased risk of treatment- and health behavior related cardiometabolic conditions among survivors of childhood cancer.