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## 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: Epigenomic Profiling of Metabolic Outcomes in Childhood Leukemia Survivors Planned research population (eligibility criteria): Acute lymphoblastic leukemia (ALL) survivors with DNA and genome-wide SNP array data (aim 2).

Proposed specific aims: 1. Determine if gene-specific DNA methylation status is associated with metabolic outcomes in ALL survivors by conducting genome-wide DNA methylation profiling 2. Identify genomic loci that play a direct role in metabolic outcomes by conducting an integrative network-based association study (INAS), which involves the joint analysis of the epigenetic and genetic data

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?: Institutional funds. CCSS Career Development Award (11/2012). R01 (2013-2014).

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.:

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

Second Malignancy:
Chronic Disease:
Psychology / Neuropsychology:
Genetics: Primary
Cancer Control: Secondary
Epidemiology / Biostatistics:
To describe the anticipated scope of the study, please indicate the specific CCSS data to be
included as <u>outcome</u> (primary or secondary) or <u>correlative factors</u> . (Check all that apply)
Late mortality:
Second Malignancy:
Health Behaviors
Tobacco: Correlative Factors
Alcohol:
Physical activity: Correlative Factors
Medical screening:
Other:
If other, please specify:
Psychosocial
Insurance:
Marriage:
Education:
Employment:
Other:
If other, please specify:
Medical conditions
Hearing/Vision/Speech:
Hormonal systems:
Heart and vascular: Secondary
Respiratory:
Digestive:
Surgical procedures:
Brain and nervous system:
Other:
If other, please specify: Primary outcomes: obesity (body mass index), diabetes (medication),
hypertension (medication), dyslipidemia (medication)
Medications

Describe medications: Medications for diabetes/insulin resistance, hypertension, and dyslipidemia
Pregnancy and offspring: Family History: Correlative Factors
Psychologic/Quality of Life
BSI-18: SF-36: CCSS-NCQ: PTS: PTG:
Other:  If other, please specify:
Chronic conditions (CTCAE v3): Health status:
Demographic
Age: Correlative Factors Race: Correlative Factors Sex: Correlative Factors Others: If others, please specify:
Cancer treatment
Chemotherapy: Correlative Factors Radiation therapy: Correlative Factors Surgery: Correlative Factors
Anticipated sources of statistical support
CCSS Statistical Center:

If local, please provide the name(s) and contact information of the statistician(s) to be involved.: Having been trained in biostatistics and epidemiology and having experience with the analyses to be conducted, I will take the lead on all statistical analyses.

Will this project utilize CCSS biologic samples?: Yes

If yes, which of the following?

Buccal cell DNA: Yes Peripheral blood: Yes Lymphoblastoid cell lines:

Second malignancy pathology samples: Other requiring collection of samples:

If other, please explain:

Other general comments: For aim 2 of the proposed project, we will leverage the genome-wide SNP array data as part of Dr. Kala Kamdar's CCSS project entitled "Genetic Polymorphisms and Metabolic Outcomes in Childhood Leukemia Survivors" to conduct an integrative network-based association study (INAS), which involves the joint analysis of the epigenetic and genetic data to identify loci that play a direct causal role in metabolic outcomes. This project will not compete or conflict with Dr. Kamdar's project. Further, Dr. Kamdar is a collaborator on this project, and I will work closely with her in the interpretation of the results.