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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?:

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)
To describe the anticipated scope of the study, please indicate the specific CCSS data to be included as outcome (primary or secondary) or correlative factors. (Check all that apply)

<table>
<thead>
<tr>
<th>Late mortality:</th>
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<tbody>
<tr>
<td>Second Malignancy:</td>
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### 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:
Local institutional statistician: Yes
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.