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: Leveraging clinical, genetic, and social determinants of health-related risk information to predict cardiomyopathy risk in African American survivors of childhood cancer

Planned research population: Five-year childhood cancer survivors participating in CCSS with genotype data
Proposed specific aims: This proposal will be led by multiple PIs (Yadav Sapkota, SJCRH; Cindy Im, UMN).

Aim 1: Develop risk prediction models for treatment-related cardiomyopathy for African American (AA) survivors of childhood cancer. Models predicting 5- and 10-year risks for cardiomyopathy across the life course, considering primary cancer treatments and conventional cardiovascular (CV) risk factors (e.g., hypertension, diabetes) will be built in data including AA survivors in the St. Jude Lifetime Cohort Study (SJLIFE), followed by incremental model-building to include informative CV biomarkers, lifestyle risk scores, and personal-/area-level socioeconomic status and deprivation measures.

Aim 2: Systematically identify genetic risk factors for cardiomyopathy and cardiac structure and function in AA survivors and evaluate their contributions to risk prediction. Using data from SJLIFE AA survivors, novel survivor-/therapy-specific polygenic risk scores (PRSs) will be constructed, including from analyses of echocardiographic measures (e.g., ejection fraction) and cardiovascular fitness (e.g., VO2 max). CV disease PRSs/rare variants from general population analyses with robust African ancestry composition will be assessed.

Aim 3: Validate risk prediction models and provide access as web-based risk calculator tools. All developed models will be validated in independent SJLIFE data, including ~400 AA survivors projected to be enrolled during the project period, for unbiased prediction performance assessment. Model generalizability will be assessed in existing independent data, with AA survivors from multi-institutional studies including CCSS. Validated models will be made broadly accessible for clinical/research use.

Secondary Aim: Aims 1-3 will be extended to predict cardiomyopathy-specific major adverse cardiovascular events (cardiomyopathy requiring heart failure medications; myocardial infarction; atrial fibrillation; CV mortality).

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?: The MPI's will submit an R01 application to fund this study

Does this project require contact of CCSS study subjects for:

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

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:

	Primary	Secondary	Correlative Factors
Insurance	-	-	✔
Marriage	-	-	✔
Education	-	-	✔
Employment	-	-	✔
Other	-	-	✔

If other, please specify: Individual-/area-level socioeconomic status variables

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: None selected

If other, please specify:

Other:

	Primary	Secondary	Correlative Factors
Pregnancy and Offspring	-	-	-
Family History	-	-	-
Chronic Conditions (CTCAE v3)	✔	-	-
Health Status	-	-	-

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:
Will this project utilize CCSS biologic samples?: Yes
If yes, which of the following?: Buccal cell DNA
If other, please explain:

Other General Comments
General comments: