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Project Requirements and Description

Requirements to submit AOI

Requirements to submit AOI (all answers must be "yes" to proceed)

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	Assessing the Efficacy of Organ System-specific Epigenetic Clocks for Predicting Treatment-related Adverse Events in Childhood Cancer Survivors
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Planned research population (eligibility criteria)

Five-year survivors of childhood cancer in the St. Jude Lifetime Cohort (SJLIFE) and Childhood Cancer Survivor Study (CCSS) with DNA methylation array and whole genome/exome sequencing or SNP array data.

Proposed specific aims

Aim 1: To evaluate organ system-specific epigenetic clocks (considering age at sample collection) as predictors of organ-specific late effects and chronic diseases in childhood cancer survivors, benchmarking against established (i.e. PCGrimAge, PCHorvath, PCHannum, and DunedinPACE) clocks.

Aim 2: To characterize the contributions of cancer treatment exposures and social determinants of health (SDOH), as well as diet and lifestyle factors at baseline measurement, to organ system-specific epigenetic age acceleration. We will also test whether these exposures modify late effect risk via their effect on organ system-specific epigenetic aging.

Aim 3: To identify genetic variation (GWAS) and genetically regulated expression (TWAS) associated with organ system-specific epigenetic age acceleration and test for gene-treatment interactions that drive epigenetic age acceleration.

Aim 4: To train a de novo set of organ system-specific epigenetic clocks using DNA methylation from childhood cancer survivors and evaluate their performance against existing clocks trained in the general population.

Will the project require non-CCSS funding to complete?

No

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? (Select all that apply)

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

Outcomes or Correlative Factors

	Primary	Secondary	Correlative Factors
Late Mortality			
Second Malignancy	✓		

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

Medical Conditions

	Primary	Secondary	Correlative Factors
Hearing/Vision/Speech	✓		
Hormonal Systems	✓		
Heart and Vascular	✓		
Respiratory	✓		
Digestive	✓		

	Primary	Secondary	Correlative Factors
Surgical Procedures			
Brain and Nervous System	✓		
Other			

If other, please specify

Medications

Describe medications

Psychologic/Quality of Life

	Primary	Secondary	Correlative Factors
BSI-18			
SF-36			
CCSS-NCQ			
PTS			
PTG			
Other			

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

CCSS Statistical Center	No
Local Institutional Statistician	No

If local, please provide the name(s) and contact information of the statistician(s) to be involved.

Will this project utilize CCSS biologic samples?

No

If yes, which of the following?

If other, please explain

Other General Comments

Agree

I agree to share this information with St. Jude

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