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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

<b>Project Title</b>	Exposure to Oil and Gas Development and Risk of Second Malignancies, Mortality, and Cardiovascular and Respiratory Events among Childhood Cancer Survivors
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### Planned research population (eligibility criteria)

All pediatric cancer survivors diagnosed with a primary malignancy between the ages of 0 and 21 and enrolled in CCSS with available SN and mortality data.

## Proposed specific aims

Aim 1. Evaluate potential associations between residential proximity to OGD and risks of developing subsequent neoplasms (SNs) among childhood cancer survivors.

Hypothesis: Survivors exposed to OGD will experience increased risk of SNs and a greater cumulative burden of SNs on average, after accounting for chemotherapy and radiation exposure during treatment.

Aim 2. Examine the influence of residential proximity to OGD on mortality risk among childhood cancer survivors.

Hypothesis: Survivors exposed to OGD will experience increased risk of mortality during follow up as compared to unexposed survivors.

Aim 3. Identify potential associations between residential proximity to OGD and incidence of self-reported respiratory and cardiovascular events among childhood cancer survivors.

Hypothesis: Survivors exposed to OGD will exhibit higher incidence of cardiovascular or respiratory event(s), even after accounting for treatments associated with these outcomes.

**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	✓		

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

If other, please specify

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## 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	Yes

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

Dr. Clark's mentorship team includes:

- Lucie Turcotte (University of Minnesota; St. Jude)
- Cindy Im (University of Minnesota; St. Jude)
- Erin Marcotte (University of Minnesota)
- Paul Nathan (Sick Kids; St. Jude)
- I-Chan Huang (St. Jude)

Despite the volume of evidence indicating that exposure to oil and gas development (OGD) is a risk factor for

pediatric cancer, cardiovascular disease, and respiratory events (1–9), little is known about the potential impacts of OGD exposure on late outcomes in childhood cancer survivors. One study to date links OGD exposure in Texas to increased mortality risk among pediatric acute myeloid leukemia and hepatoblastoma survivors (10). We will build on this work by using the Childhood Cancer Survivor Study (CCSS) cohort to evaluate the influence of residential OGD exposure on risk of subsequent neoplasms, mortality, and cardiovascular and respiratory events among pediatric cancer survivors.

Dr. Clark (PI) has expertise in environmental epidemiology and cancer etiology with more than fifteen publications on the environmental and public health impacts of extractive industries (e.g., 11–15). She led one of the largest studies of OGD and pediatric cancer risk to date, finding that proximity to OGD was associated with 2-3 times the odds of acute lymphoblastic leukemia in Pennsylvania children (11). Dr. Clark provided expert testimony to the Pennsylvania House of Representatives on OGD exposure and pediatric cancer risk, and has served as a topic area expert in the U.S. Environmental Protection Agency's "2023 Draft Supplement to the Risk Evaluation of 1,4-Dioxane." Her expertise in this area is recognized, and she is well-prepared to lead the proposed work.

Although Dr. Clark plans to complete this work even if unfunded, she plans to submit part of this work to the Rally Foundation and to any available St. Jude career development awards.

## References

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13. Clark, C. J. et al. Community concern and government response: Identifying socio-economic and demographic predictors of oil and gas complaints and drinking water impairments in Pennsylvania. *Energy Res. Soc. Sci.* 76, 102070 (2021).
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**Agree**

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