New Cohorts for Environmental Exposures and Cancer Risk (CEECCR; UG3/UH3) & CEECCR Coordinating Center (U24)

Pre-Application Webinar, Nov. 10, 2020
Somdat Mahabir, Ph.D., M.P.H.
Using WebEx and Webinar Logistics

- Submit questions at any time using the Chat Panel and select **Host**
- You may need to activate the appropriate box using the floating navigation panel. Found on the center of your screen
- This webinar is being recorded
- To connect to the audio, you may have the system call you by entering your telephone number including area code and selecting “Call Me” OR by dialing in to the session at:
  - 1-650-479-3207
  - Access Code: 172 258 4128
Webinar Presenter

Somdat Mahabir, Ph.D., M.P.H.
Program Director, Environmental Epidemiology Branch,
Epidemiology and Genomics Research Program,
Division of Cancer Control and Population Sciences
National Cancer Institute

https://epi.grants.cancer.gov/staff/mahabir.html
Purpose

- RFA CA-20-049 (UG3/UH3) will support approx. 5 new research-based cancer etiology cohorts that use innovative strategies and approaches to address:
  - Gaps between environmental exposures, genetics, and other molecular factors and cancer etiology
  - Ensure rigor and reproducibility by encouraging standardized collection of biospecimen and set of core data across cohorts
  - Racial, ethnic, and geographic disparities
- RFA CA-20-050 (U24) will support a Coordinating Center to facilitate coordination among the new prospective cohorts supported under RFA CA-20-049
Goal

- Fund approximately five new research-based prospective cohorts:
  - Assess new and understudied exposures with innovative measures
  - Focus on both short-term and longer-term research questions
  - Investigators required to collaborate – facilitated by Coordinating Center
  - Priority for the research aims and innovation on methods to achieve those aims – overarching priority on unanswered research questions related to environmental exposures and their public health importance
**Need for New Etiology Cohorts**

- Environmental exposures (e.g., new exposures, persistent chemicals, and chemical mixtures) understudied
- IARC and NTP have identified several “Group 1” or “Known Carcinogens” to humans, but many more environmental exposures lack adequate evidence to properly classify
- Identification of the key carcinogenic hallmarks of environmental exposures needed in prospective designs
- Challenge with existing cohorts – aging cohorts; remaining blood samples cannot address current and emerging gaps related to environmental exposures; limited research on life-course exposures; diversity of populations by geography and race/ethnicity

*Resources of existing cohorts (data and biospecimens) -- R01/R21/R03 applications*
Short-Term Research Examples

- Use IARC framework to assess biological mechanisms to support classification of environmental exposures
- Other bioassays
- Building new cohorts
- Use incident cases for case-control/case-cohort studies in the initial years

<table>
<thead>
<tr>
<th>Biological Mechanisms (Carcinogenic characteristics)</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic activation</td>
<td>DNA and Protein Adducts</td>
</tr>
<tr>
<td>Is genotoxic</td>
<td>DNA damage; Gene mutations, Cytogenetic changes</td>
</tr>
<tr>
<td>Induces chronic inflammation</td>
<td>Elevated WBC; altered cytokine/chemokine production</td>
</tr>
<tr>
<td>Is immunosuppressive</td>
<td>Decreased immunosurveillance; immune dysfunction</td>
</tr>
<tr>
<td>Alters cell proliferation</td>
<td>Cell proliferation; Angiogenesis</td>
</tr>
</tbody>
</table>

Smith et al. Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. Env Health Persp 124(6):713-21, 2016
Longer-Term Research Questions

- What persistent chemicals in the environment affect cancer risk in populations across various geographic areas (e.g. rural, urban)?
- What chemical, physical, lifestyle and genetic factors interact to affect cancer risk in understudied populations?
- How are timing of environmental exposures, multiple exposures, and chronic low-dose exposures associated with cancer development?
Coordinating Center (U24)

- Biospecimen and data collection
- Standard Operating Procedures
- Communication & Meeting support
- Project website
- Support data harmonization
- Coordinate assessment across cohorts
- Facilitate deposition of data to NIH
RFA CA-20-049: Study Requirements for New Cohorts

- Scientific justification of the research gaps to be addressed in both exposures and outcomes;
- Evidence of validity and reproducibility of proposed exposure assessments and outcome measures;
- Evidence of community engagement in the development and conduct of proposed research;
- Willingness to collaborate on a core set of data related to environmental exposures and cancer etiology;
- Description of critical milestones, performance metrics, and timeline for completion of milestones;
- Description of sustainability and preservation of cohort resources that extend beyond the life of the award;
- Include data/resource sharing plan.
RFA CA-20-050: Responsibilities of the Coordinating Center

- The U24 Coordinating Center will operate as supporting infrastructure for the CEECR Program, assisting and supporting the new prospective cohorts under RFA CA-20-049
  - Provide a centralized administrative infrastructure
  - Provide administrative and logistical support for CEECR activities (example, provision of public website for communication)
  - Create standard operating procedures (SOPs) and best practices for the collection of common data/biospecimen elements
  - Facilitate deposition of data to NIH repositories
  - Facilitate communication and meeting support
UG3/UH3 Research Mechanism

- **UG3 phase:** PI sets milestones for recruitment and data collection
  - Requires approval from NIH (after selected for funding, before NOA)
  - Cap for UG3 phase: $750K direct cost for each year in years 1 and 2
- **UH3 phase** focused on completing research – not guaranteed
  - No cap for UH3 phase: budget must only reflect work needed to accomplish the aims

**UG3/UH3 Process**

**Pre-Award**
- Discussion of PI-set milestones with NCI

**UG3 Phase**
- 2 years
- Must show feasibility/meet milestones:
  - Recruitment
  - Data Collection

**Transition (NCI approval)**

**UH3 Phase**
- Up to 4 years
- Complete: Recruitment Data Collection & analysis Manuscript preparation
UG3/UH3 and U24 are cooperative mechanisms

These mechanisms facilitate:

- NIH additional involvement
- Additional oversight of awarded grants
- Collaborative work among awardees
- Access of research resource to extramural community
- In-person or virtual meeting in all years
Non-Responsive Applications (RFA-CA-20-049)

- Approaches that do not include human populations;
- Approaches that are based on secondary use of existing cohort data;
- Approaches that use a study design that will not lead to a prospective cohort;
- Applications from foreign countries that do not show direct relevance to the U.S. population (applications for foreign countries are eligible but must show relevance to U.S. populations); and
- Non-compliant data/resource sharing plans and not following FAIR principles.
Next Steps

- A recording of the webinar slides and FAQs will be posted to: https://epi.grants.cancer.gov/cohorts/
- If you have questions, please contact Somdat Mahabir mahabir@mail.nih.gov or Abee Boyles abee.boyles@nih.gov
- Application due date: January 29, 2021
- Letter of Intent due on December 15, 2020
- Good luck!
Pre-submitted Questions

How should applications organize specific aims in the UG3/UH3 phases?

Applicants must provide the overall goals for the entire application and indicate separately Specific Aims to be accomplished in the UG3 and UH3 phases.

Why is NCI funding new cohorts only?

This RFA for research-driven risk cohorts is responsive to NCAB. Existing cohorts, while important have limitations to address current and emerging gaps related to environmental exposures.
Pre-submitted Questions

*What are the core set of data and biological specimens to be collected?*

Will be decided at the first annual meeting of the CEECR Program, which will include the cohorts, the Coordinating Center and NIH.

*Can methodological research be built into the cohorts in the short-term?*

Yes.

*What is the population sample size being anticipated?*

Sample size, types and frequencies of biological sample collection will be driven by the science proposed.
Pre-submitted Questions

Is the RFA CA-20-049 and RFA CA-20-050 going to be reissued?
These RFAs currently have one application due date – January 29, 2021.

Are foreign institutions allowed to apply? What about international partners and/or subcontracts?
Yes, foreign institutions or studies based in foreign countries are eligible. However, priority will be given to studies with direct relevance to U.S. populations.
Acknowledgement

- **Planning & Development Team:** Somdat Mahabir, Gary Ellison, Scott Rogers, Joanne Elena, Nonye Harvey, Pothur Srinivas, Kathy Helzlsouer

- **Management Team:** Somdat Mahabir (NCI Lead), Abee Boyles (NIEHS Lead), Curt Dellavalle, Gila Neta

- **Environmental Epidemiology Branch, NCI/DCCPS/EGRP**