CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

REQUEST FOR APPLICATIONS

RFA R-23.2 Connect

The Texas Connect for Cancer Prevention Study:

A Prospective Cohort to Study Cancer Etiology, Prevention, and Early Detection

Please also refer to the Instructions for Applicants document, which will be posted on January 25, 2023

Application Receipt Opening Date: January 25, 2023

Application Receipt Closing Date: April 18, 2023

FY2023
Fiscal Year Award Period
September 1, 2022-August 31, 2023

TABLE OF CONTENTS

RFA VERSION HISTORY

Rev	01/17/23	RFA released

1. KEY POINTS

- Supports applications to recruit 25,000 to 35,000 adults (40 to 65 years of age) into a prospective, longitudinal, multicenter study within integrated health care systems (IHCSs) in the United States as a participating site in the NCI Connect for Cancer Prevention Study (https://github.com/episphere/connect/wiki; see also the public site at https://www.cancer.gov/connect-prevention-study/) to provide a powerful platform to study cancer etiology, prevention, and early detection.
- Applicants may request a maximum of $1,500,000 per year for a 5-year period.
- Multi-Principal Investigators (PIs) (MIs) are not allowed under this RFA, although Coinvestigators (Co-Is) may be included.
- Note that CPRIT does not allow the use of the term Co-PI.
- Minimum effort for the PI throughout the project period is required.

Note that key sections of this RFA are adapted from the NCI Connect for Cancer Prevention Study (IRB #000034, NCT04609072), available under *Current Funding Opportunities* for Academic Research in CARS.

Applicants are encouraged to review the IRB protocol (https://github.com/episphere/connect/blob/master/about%20connect/connect_protocol_v1.5_07212021_clean.pdf) for detailed information on Connect study design, study assessment and procedures, statistical considerations, regulatory and operational considerations, governance structure, and other considerations.

- The Connect study is run by the Coordinating Center within the NCI Division of Cancer Epidemiology and Genomics (DCEG), with support services provided by the National Opinion Research Center at the University of Chicago (NORC). Four initial awards have been established to set up recruitment at 9 individual IHCSs:
    1. Henry Ford Health with Health Partners and Marshfield Clinic Health System
    2. Kaiser Permanente Colorado with Kaiser Permanente Georgia, Kaiser Permanente Hawaii, and Kaiser Permanente Northwest
    3. Sanford Health
    4. The University of Chicago Medicine and Comprehensive Cancer Center

- One or more sites in Texas will be funded by CPRIT and will participate as full members of the Connect study. The NCI DCEG Coordinating Center will establish a collaborative agreement with participating institution(s) in Texas and will assist with field activities, such as developing standard operating procedures (SOPs) and the manual of operating procedures (MOOPs), as well as training research staff to implement the MOOPs. NORC will also provide Helpdesk support, conduct linkages, and aid efforts to follow participants who leave the IHCS.
- **Structure and Governance of Connect Study.** The Connect study organizational structure is described in Appendix 1 of the Connect Study Protocol (#000034), and includes leadership committees, the DCEG Steering Committee and Executive Committee, as well as the Resource Access Committee (RAC), which are supported by the functions of the Coordinating Center, as well as external guidance from the International Scientific Advisory Board and the Connect Patient Advisory Board. Scientific review of the Connect study will be conducted by the DCEG Senior Advisory Group.
- **Institutional Study Team**. Key personnel may include PI, Co-I or Project Manager, Programmer(s), Biospecimen Collection Manager/Study Manager, and Research Assistants/Phlebotomists. Select responsibilities of the study team are summarized in Table 1.
- **Responsibilities of Participating Institution**
    - Institution must be willing and able to utilize the NIH IRB.
    - Institution must be willing to provide electronic medical record (EMR) or insurance claims data broadly defined to include medical history, medical imaging, and any other health-related data such as pathology reports and insurance claims data among study participants who provide HIPAA authorization to NCI using a secure file transfer protocol server with data encrypted in transit and during rest.

- Institution must be willing to allow and facilitate use of the EMR to contact patients for recruitment and enrollment in routine questionnaires and sample collection, etc, through patient access portals, eg, MyChart, and provide demographic information including age, race and ethnicity, and sex (male/female at birth or current) among all people invited to the study.

Table 1. Select Responsibilities of Participating Study Team

Team Member	Responsibilities (abbreviated list)
Site PI & other senior leadership	○ Identify clinical champions to promote Connect ○ Contribute to development of study enhancements
Programmers	○ Develop algorithms with EMR data to identify and verify eligible patients ○ Connect to existing application programming interfaces (APIs) for bidirectional data transfer ○ Transfer EMR data via file transfer protocol
Study & Biospecimen Manager(s)	○ Customize template SOPs ○ Customize recruitment assets ○ Collaborate on enhanced recruitment strategies
Research Assistants/ Phlebotomists	○ Navigate participant through biospecimen collection ○ Draw and ship blood or other biospecimens

- **Future Use of Stored Specimens and Data.** Biological specimens will be stored temporarily at appropriate temperatures at the collection facilities, eg, study site, until transferred to the Connect processing facility (Frederick National Laboratory operated currently by Leidos Biomed) for permanent storage. Deidentified study data, such as survey or EMR data, and biospecimens (collectively referred to as the "Connect Resource") will be available for the research community through a continuum of open to controlled access mechanisms, managed by the Connect Resource Access Committee (see IRB Protocol #000034, Appendix 1 *Study Governance Structure*) and available on the Connect Data Platform. Scientific researchers will be able to request access through a multistep process coordinated by the DCEG Connect Coordinating Center and directed by the RAC. Researchers with projects approved by the RAC will be able to access individual-level data and specimens after receiving IRB approval, if required, and signing

a Data Transfer Agreement and/or Materials Transfer Agreement as appropriate with the NCI. **It is understood that institutions may also be conducting other IRB-approved studies, including other cohort studies, and that some participants in Connect may also be participating in other institutional studies.**

- The study population consists of patients or members of participating IHCS at the time of enrollment with no personal history of cancer and aged between 40 and 65 years old at study invitation. **The enrollment of ethnic and racial minority populations, particularly Latino men and women, is a high priority for participating sites in Texas.**

2. ABOUT CPRIT

The State of Texas has established the Cancer Prevention and Research Institute of Texas (CPRIT), which may issue up to $6 billion in general obligation bonds to fund grants for cancer research and prevention.

CPRIT is charged by the Texas Legislature to do the following:

- Create and expedite innovation in the area of cancer research and in enhancing the potential for a medical or scientific breakthrough in the prevention of, or cures for, cancer;
- Attract, create, or expand research capabilities of public or private institutions of higher education and other public or private entities that will promote a substantial increase in cancer research and in the creation of high-quality new jobs in the State of Texas; and
- Develop and implement the Texas Cancer Plan.

2.1. Academic Research Program Priorities

The Texas Legislature has charged the CPRIT Oversight Committee with establishing program priorities on an annual basis. These priorities are intended to provide transparency with regard to how the Oversight Committee directs the orientation of the agency's funding portfolio.

Established Principles:

- Scientific excellence and impact on cancer
- Increasing the life sciences infrastructure in all regions of the state
- Achieving health equity and reducing cancer disparities

The program priorities for academic research adopted by the Oversight Committee include funding projects that address or utilize the following:

- Recruitment of outstanding cancer researchers to Texas
- Investment in core facilities
- A broad range of innovative, investigator-initiated research projects
- Implementation research to accelerate the adoption and deployment of evidence-based prevention and screening interventions
- Computational oncology and analytic methods
- Childhood and adolescent cancers
- Hepatocellular cancer
- Expanding access to innovative clinical trials

3. BACKGROUND AND RATIONALE

This section has been adapted from the Connect IRB protocol (#000034).

3.1. Background

Over 1.9 million people in the United States had a diagnosis of cancer in 2022, and over 609,00 people died of cancer-related causes. Nationally, this places cancer as the second leading cause of death, after cardiovascular diseases. Although treatments for cancer are improving and there are promising advances through personalized medicine, the total number of cancer diagnoses is expected to increase substantially over the next decade, in large part due to the aging of the population and behavioral/lifestyle changes. The risk of developing cancer depends on the complex interplay of multiple factors, including our genes; age and gender, lifestyle, and behavioral factors such as diet, energy balance, physical activity, tobacco, and alcohol; endogenous factors such as hormones and growth factors; medication and drug use; infectious agents; and exposures in our surrounding environment and workplace. Therefore, research on the causes of primary and second cancers as well as prevention strategies are critical to reduce the burden of cancer in the population.

Given the changing nature of most cancer-related exposures over time and over an individual's lifespan, a prospective cohort study design, ie, a longitudinal study to determine how carcinogenic changes unfold over time (through detection of early lesions of cancer and changes

in biomarkers), is essential to make progress in our understanding of the causes of cancer. Ascertainment of disease diagnoses, treatment courses, laboratory tests, and other outcomes in prospective cohort studies in the United States is logistically very complex and expensive due to the lack of an organized health care system with comprehensive coverage, as exists in many other countries with government-run health care systems. IHCSs (formerly called HMOs) are the exception. These organizations have several important characteristics including provision of comprehensive health care to their members through a range of coordinated health care facilities and services, and storage of all health care information on their members in a central database. The existing infrastructure provides a highly efficient setting for the proposed new cohort. Major advantages of IHCSs include the availability of comprehensive EMRs, a passive follow-up system that is both cost effective and highly complete, existing clinical infrastructure for specimen collection, and the long-term stability of the population.

3.2. Rationale

The central focus of the Connect cohort is to understand the etiology and natural history of cancer to inform new approaches in precision prevention and early detection of cancer. A number of recent developments in the assessment of external and internal exposures, as well as tissue characterization, provide unprecedented opportunities to advance the field of cancer epidemiology and prevention. Most notably, these include the following:

- Widespread use of electronic devices and applications in the digital age that facilitate engagement of study participants to provide and receive health information;
- Opportunities for high-quality exposure assessment using innovative technologies such as wearable devices to measure behavior and environment;
- Increased availability and quality of EMR and medical imaging for assessment of health conditions and medications;
- New, cost-effective methodologies to interrogate the genome, epigenome, transcriptome, proteome, metabolome, microbiome, and other biological processes;
- Increased availability and quality of databases for data linkages, including pollution monitoring, pharmaceutical records, and cancer registries; and
- Advances in molecular profiling of tumors and precursor lesions to study the natural history of cancer and etiologic heterogeneity across tumor subtypes.

These technologies coupled with new methods in complex analytics of integrated high-dimensional data provide powerful tools to address the primary objectives of the Connect study (see section 4.2, Primary Objectives).

Key characteristics of the Connect cohort (Figure 1) designed to address a broad range of scientific questions related to cancer include the following:

Figure 1. Study Design Features for Connect for Cancer Prevention Study

1. Large sample size to identify a sufficient number of participants who develop incident cancer.
2. Serial exposure assessment and biological specimen collections to study changing exposures/biomarkers and evaluate critical exposure windows prior to disease diagnosis.
3. Collection and storage protocols for biological specimens that are adequate for new assays and technologies.
4. Longitudinal (which may include retrospective) access to EMRs to obtain information on medication use, medical conditions, medical screening, and medical (including cancer) diagnoses.
5. Longitudinal (which may include retrospective) collection of tissue specimens from malignant tumors as well as benign or precursor lesions to study the natural history of cancer and molecular subtypes of cancer.

This state-of-the-art cohort employs an efficient, flexible, and integrated cloud-based infrastructure that utilizes modern interoperability standards to serve as a research workhorse for future generations of scientists. Although the primary end points of interest for this cohort are cancer incidence and mortality, the infrastructure will be designed to also enable collaborative studies of general research use and ancillary enhancements. **This RFA solicits applications for CPRIT-supported participation of a Texas institution(s) as member of the Connect study with the long-term potential to identify social, environmental, behavioral, and genetic factors that underlie cancer risk among Texans.**

4. RESEARCH OBJECTIVES

CPRIT will support a recruitment site(s) in Texas to participate in the Connect study, a prospective cohort to understand the etiology and natural history of cancer to inform new approaches in precision prevention and early detection of cancer. The objectives identified in the Connect study (IRB Protocol #000034, NCT04609072) are provided below.

4.1. Objectives

The overarching objective is to recruit approximately 200,000 adults into a prospective, multicenter study within IHCSs in the United States to provide a powerful platform for studying the etiology, prevention, and early detection of cancer (Table 2).

Table 2. Objectives of the Connect Study.

OBJECTIVES	END POINTS	JUSTIFICATION FOR END POINTS
Primary		
The **overarching objective** is to recruit 200,000 adults aged 40 to 65 years into a prospective, multicenter study within IHCSs in the United States using a powerful digital platform. The **primary objective** is to study associations of end points in the cancer continuum with multilevel factors, including behavioral, biological, environmental, medical, and social factors.	Cancer transformation, incidence, progression, and mortality end points could include, but are not limited to • early biological effects (eg, inflammation or metabolomic markers) related to cancer • intermediate biomarkers • cancer precursors • cancer incidence • cause of death • cancer survival, risk of second cancers and survivorship	These end points will facilitate inferences on **cancer etiology and natural history** to provide insights into carcinogenic processes and inform new approaches **in risk assessment** and **early detection of cancer** (see below for additional detail). Studying the cancer continuum will improve translation of epidemiologic findings to public health and clinical practice.
Secondary		
The **secondary objective** is to create a publicly available resource of deidentified data and biological sample repository to registered users for general research use.	The end points are numerous and could include methodological research, human biology, ancestry, evolution, or health-related outcomes.	The Connect study is a rich resource that will benefit the progress of science for years to come.
Tertiary/Exploratory		
Not applicable		

4.2. Primary Objectives

Etiology of Cancer: This prospective cohort will enable studies to identify and characterize biological, behavioral, and (broadly defined) environmental risk factors and the interactions among them associated with the incidence of different cancers. Specifically, serial exposure and biomarker assessments in individuals prior to any cancer diagnosis will allow the study of how changes over many years could influence cancer development and the identification of critical exposure periods. Examples of research topics in this area include the following:

- Evaluation of current and emerging behavioral and environmental factors, eg, vaping, physical activity patterns, in relation to cancer risk and progression.
- Evaluation of possible links between commonly used pharmaceuticals and medical procedures, eg, opioid use, gastric bypass surgery, with subsequent cancer risk.
- Investigation of the relationship between exposure to outdoor air pollution (including at the home) and cancer risk, based on linkage of the residential address to modeled estimates of air pollutants derived from Environmental Protection Agency's air quality monitoring network.
- Investigation of the relationship between ingested drinking water contaminants and cancer risk, based on linkage of the residential address and self-reported public drinking water utility to regulatory monitoring data for water contaminants.
- Characterization of biomarkers of exposure, eg, pollutants, and early biological effects, eg, inflammation markers, metabolomic markers, to determine distribution in the population, sources of variation and changes over time.
- Identification of biomarkers of susceptibility and early biological effects in tumor initiation to characterize biological processes including the genome, eg, germline genetic susceptibility factors, epigenome, transcriptome, proteome, metabolome, microbiome, and immune response as well as their interactions with behavioral, contextual, and environmental factors.
- Identification of molecular signatures in cancers and precursors associated with behavioral, contextual, and environmental factors as well as germline-somatic associations to provide insights into mechanisms of carcinogenesis.
- Characterization of etiologic heterogeneity for different tumor subtypes using state-of-the-art imaging and molecular characterization of tumor and relevant tissues.

Natural history from precursor to tumor transformation: Although cancer initiation is typically not observable, precursor lesions detected through population-based screening programs or clinical symptoms have been identified for certain cancer types (eg, breast, cervical, colorectal cancers). Some cancer precursors are typically removed at detection to prevent progression to cancer, eg, cervical cancer precursors and colorectal polyps. Others, eg, hematological cancer precursors, atypical hyperplasia of the breast or the uterus, or anal cancer precursors, can be left and observed through clinical surveillance. This allows for a direct observation of the possible transition from precursor to early-stage cancer that can be detected and treated with improved prognosis. Clinical imaging data, eg, ultrasound of the breast from screening programs or symptomatic conditions, can also detect abnormalities that represent cancer precursors. For many cancer sites, precursors are not well characterized and typically are not detected widely.

- Study of biomarkers of tumor transformation and progression, including early postzygotic mutational events, eg, clonal mosaicism, clonal hematopoiesis, high-risk molecular changes in precursor lesions, eg, benign breast disease, colon polyps, cervical cancer precursors, lung nodules, esophageal metaplasia/dysplasia, endometrial hyperplasia, urothelial proliferation/dysplasia.
- Identification of precursors for cancers with suspected or unknown precursors, eg, monoclonal gammopathy of undetermined significance (MGUS) and hematological cancers.
- Identification of determinants of cancer precursors, eg, behavioral, contextual, environmental, and genetic, to inform natural history studies and models for predicting clinically relevant cancer precursors.

Cancer Risk Assessment: Determining individual risk of cancer is important for public health, eg, population-based cancer screening programs and individual counseling for cancer prevention and early detection strategies. During the last decade, major progress has been made in the development of statistical methods and the application of risk prediction models of various cancer sites. The Connect study resource will be instrumental in the development and validation of risk prediction models for precision prevention through the integration of risk factors from multiple sources, eg, questionnaires, EMRs, imaging, personal monitors, germline genetics, and

blood/urine/tissue biomarkers, accounting for changes over time and more precise definitions of end points, eg, molecular subtypes of cancer. Integral to these risk prediction efforts, the study questionnaire has been developed to provide relevant risk factor information for many cancer end points. As new risk factors are identified, they can be integrated into follow-up questionnaires to allow for continuous updating and improvement of cancer risk prediction models.

Early Detection of Cancer: Early detection of cancer promises to improve cancer outcomes through detection of early-stage cancers and identification of precursors that can be treated to avoid development of invasive cancers. Currently, very few early detection approaches, eg, blood biomarkers or imaging, exist that have demonstrated improved cancer outcomes in clinical trials. Repeated biomarker measurements using specimens collected prior to diagnosis of cancer from study participants will provide extensive opportunities to identify biomarkers, eg, mutations in prediagnostic circulating tumor DNA, and develop algorithms for the early detection of cancer based on the trajectories of high-dimensional biomarkers. Studies of early detection marker development can be conducted in Connect, including marker discovery, assessment of clinical performance for detection of disease, and evaluation of detection windows and lead time for specific markers and cancer sites, as well as comparative studies of cancer detection for several early detection approaches.

Secondary Aims

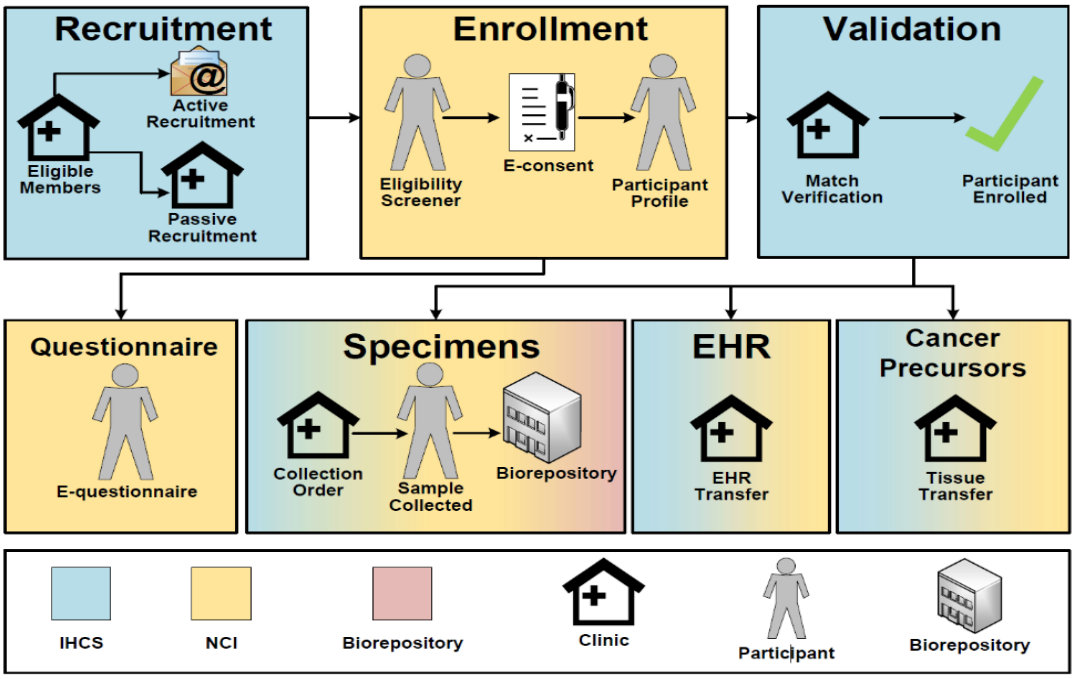
The Connect cohort will be a large and comprehensive data resource and biospecimen repository for general research use.

5. STUDY DESIGN

The Connect study is a multisite, prospective cohort study with the goal of enrolling 200,000 adults free of cancer who are patients or members of participating IHCSs in the United States (see section 6.1. Inclusion Criteria). Due to the long natural history of cancer, the Connect study anticipates following participants for life. Participants will have consented to passive study activities and to participate in active study activities at baseline and regular intervals throughout follow-up (see Figure 2). During follow-up, other ancillary studies also might be proposed to participants. Study activities and communication with participants will be facilitated by a secure,

web-enabled participant application that has been developed by the NCI DCEG Connect Coordinating Center ("participant app").

Figure 2. Participant Workflow for Connect Cohort



- **Baseline Activities**. After providing informed consent, the study participants will be asked to complete the following baseline study procedures:
  - Participant profile and match verification (see Connect IRB Protocol #000034, Section 5.6 *Strategies for Recruitment and Retention*)
  - Baseline questionnaire divided into 4 modules to capture behavioral, medical, residential history, social, and identifying information (social security number [SSN] will be requested but not required) (see Connect IRB Protocol #000034, Section 7.2 *Clinical Evaluations*)
  - Blood, urine, and mouthwash specimen collection and associated questionnaires (see Connect IRB Protocol #000034, Section 7.3 *Biospecimen Evaluations*)
  - HIPAA authorization for the collection of EMR and other IHCS data (see Connect IRB Protocol #000034, Section 7.2 *Clinical Evaluations*) and acquisition of tissues for prevalent cancer precursors (see Connect IRB Protocol #000034, Section 7.3 *Biospecimen Evaluations*)

- **Passive Follow-up Activities:**
  - EMR updates: EMR data will be released by the IHCS and any other health care providers to NCI at least once a year as long as the participant remains in the IHCS (see Connect IRB Protocol #000034, Section 7.2 *Clinical Evaluations*). Cancer, mortality, and other health outcomes, as well as exposure information, eg, weight, will be ascertained from the EMR.
  - Clinical tissue specimen collection: Precursor and cancerous lesions will be requested from the participating IHCS or affiliated facilities.
  - Data linkages: For all participants (including those who leave the IHCS), personal identifiable information, including name and SSN, will be linked to data from US state cancer registries and the National Death Index (NDI) to ascertain end points, including cancer and vital status. Linkage with state registries will be facilitated, where applicable, by the Virtual Pooled Registry Cancer Linkage System (VPR-CLS), an initiative from the North American Association of Central Cancer Registries (NAACCR) and the NCI Division of Cancer Control and Population Sciences to provide a central and streamlined application process for cancer surveillance data linkages. Other data linkages may include geocoding to environmental monitoring databases and demographic and health data, such as census, Medicare, human immunodeficiency virus (HIV) registries, pharmacies, and imaging centers.
- **Active follow-up activities:**
  - Serial questionnaires on changes in health status and end points as well as existing and new exposures, including quality of life and lifelong cancer screening behaviors (see Connect IRB Protocol #000034, Section 7.2 *Clinical Evaluations*)
  - Serial biospecimen collections from time to time as needed (see Connect IRB Protocol #000034, Section 7.3 *Biospecimen Evaluations*)
  - EMR updates: For participants who leave the IHCS, the Connect Study will request that they provide the EMR data through the participant application.
  - Additional assessments: Participants will be asked to use their own devices and/or be provided with a device, such as wearable devices or applications for mobile devices (provided by the NCI DCEG Coordinating Center). During follow-up, other possible

technology-assisted assessment tools may include those that measure heart rate, pulse oximetry, ambient air pollutants, and other assessments.

6. STUDY POPULATION

6.1. Inclusion Criteria

Due to the minimal risk nature of the Connect protocol, all individuals interested and able to participate in Connect, who meet the eligibility criteria and are not specifically excluded, will be able to participate. To be eligible to participate in this study, an individual must meet all of the following criteria:

- Patients or members of participating IHCS at the time of enrollment.
- Age between 40 and 65 years old without a personal history of cancer at study invitation.
- Children are not included in Connect because cancer incidence is low.

6.2. Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study:

- Individuals with a history of invasive cancer (other than nonmelanoma skin cancer).
- Individuals with known cognitive impairment documented in their medical record.

6.3. Active recruitment outreach of underrepresented populations

A major goal of this RFA is to recruit underrepresented individuals who are representative of the Texas population. In parallel, the Connect study seeks to increase the proportion of Hispanic participants. The successful applicant is expected to demonstrate the ability to recruit a diverse population and to describe health system members and patients who are in underrepresented populations within the health system's catchment areas, eg, non-White individuals, living in medically underserved areas, as well as efforts to recruit such individuals. Such efforts can include research coordinators traveling to clinics in underserved areas, tailored recruitment materials, and community outreach activities.

Please refer to the Connect for Cancer Prevention Study (Protocol #000034) for additional information on study design, such as recruitment and retention (Section 5.6) participant

discontinuation/withdrawal (Section 6), study assessments and procedures, and correlative studies for research (Section 7).

6.4. Sample storage, tracking and disposition

Biological specimens will be stored temporarily at appropriate temperatures at the collection facilities, eg, study site, or participant's home, eg, refrigerated, ambient, until transferred to the Connect processing facility (Frederick National Laboratory operated currently by Leidos Biomed). Shipment procedures are outlined in the SOPs to maintain the cold chain needed to prevent specimen degradation. Specimens collected by participants at home will be shipped directly to the Connect processing facility. Tracking of the biological specimens will be done by the IHCS and the Connect processing facility through the study data system. The samples obtained under this protocol will be stored indefinitely at appropriate temperatures at the Connect central repository (Frederick National Laboratory operated currently by Leidos Biomed). Refer to the NCI Connect Study IRB Protocol, #000034, for information on disposal of biological specimens upon revocation of consent and withdrawal from the study (Section 7.3 *Biospecimen Evaluations*). Deidentified study data, such as survey or EMR data, and biospecimens (collectively referred to as the "Connect Resource") will be available for the research community through a continuum of open to controlled access, managed by the Connect Resource Access Committee (see IRB Protocol, Appendix 1 *Study Governance Structure*) and available on the Connect Data Platform.

6.5. Compensation

Monetary and nonmonetary compensation will be provided for completing study activities. At baseline, monetary compensation will include parking reimbursement (where applicable) plus compensation of $25 after completion of the 4 questionnaire modules and donation of the blood sample. During each follow-up contact for biospecimen collection, compensation of no more than $25 will be provided. In addition, participants might be given the option to receive nonmonetary compensation, eg, data summaries from questionnaires such as diet composition, or branded study materials, eg, pens, pins, tote bags provided by the NCI DCEG Coordinating Center. Note that the NCI Support Services contractor administers the compensation and incentives through the MyConnect participant site; providing compensation(s) is not a responsibility of the participating sites.

8. FUNDING INFORMATION

Applicants may request a maximum of $7,500,000 in total costs for up to 5 years for recruitment of study subjects. Exceptions to these limits may be requested if extremely well justified (see section 12.5.8). Funds may be used for salary and fringe benefits; research supplies; printing supplies and study materials such as mailed invitations, brochures, banners, etc; equipment; subject participation costs; and travel to scientific/technical meetings or collaborating institutions. **Note that the NCI DCEG Coordinating Center will cover the costs of the Helpdesk (via the support services contractor), participant incentives, biospecimen collection tubes/containers, shipping supplies, cancer registry, and other linkages to the Connect databases.** Requests for funds to support construction and/or renovation will not be approved under this funding mechanism. State law limits the amount of award funding that may be spent on indirect costs to no more than 5% of the total award amount.

9. ELIGIBILITY

- The applicant must be a Texas-based entity. Any health care provider that conducts research is eligible to apply for funding under this award mechanism. Ascertainment of disease diagnosis, treatment courses, laboratory tests, and other outcomes in a longitudinal, prospective cohort study is complex, and the applicant must maintain an integrated health care system, ie, an HMO, or an integrated network providing comprehensive health care to their members through a range of coordinated health care facilities and services, and storage of all health care information on their members in a central database (EMR).
- The applicant institution must maintain a cancer registry and have infrastructure for archived tissue specimens and biospecimen collection facilities in a clinical or research setting.
- The applicant institution must have a diverse, ideally large, catchment population.
- The PI must have a doctoral degree, including MD, PhD, DDS, DMD, DrPH, DO, DVM, or equivalent, and must be a full-time resident of Texas during the time the research that is the subject of the grant is conducted.
- This award mechanism does not allow for MIs.

- Any PI on the Connect study is required to maintain a minimum 20% level of effort throughout the entire award period. The level of effort of the PI and Co-I (if applicable) must be substantial, together summing a minimum of 50% throughout the entire award period. If the application does not have a Co-I then the PI must maintain a minimum 50% level of effort throughout the entire award period.
- A PI may submit only 1 application under this RFA during this funding cycle.
- A PI may be a part of only 1 application under this RFA.
- An individual may serve as a PI on no more than 3 active CPRIT Academic Research grants. Recruitment Grants and Research Training Awards do not count toward the 3-grant maximum; however, CPRIT considers MIRA Project Co-PIs equivalent to a PI. For the purpose of calculating the number of active grants, CPRIT will consider the number of active grants at the time of the award contract effective date (for this cycle expected to be August 31, 2023).
- Collaborating organizations may include public, not-for-profit, and for-profit entities but must be a component of the applicant institution's IHCS and located within Texas.
- An applicant is eligible to receive a grant award only if the applicant certifies that the applicant institution or organization, including the PI, any senior member or key personnel listed on the grant application, or any officer or director of the grant applicant's institution or organization (or any person related to 1 or more of these individuals within the second degree of consanguinity or affinity) has not made and will not make a contribution to CPRIT or to any foundation specifically created to benefit CPRIT.
- An applicant is not eligible to receive a CPRIT grant award if the applicant PI, any senior member or key personnel listed on the grant application, or any officer or director of the grant applicant's organization or institution is related to a CPRIT Oversight Committee member.
- The applicant must report whether the applicant institution or organization, the PI, or other individuals who contribute to the execution of the proposed project in a substantive, measurable way, whether or not those individuals are slated to receive salary or compensation under the grant award, are currently ineligible to receive federal grant funds or have had a grant terminated for cause within 5 years prior to the submission date of the grant application.

- CPRIT grants will be awarded by contract to successful applicants. Certain contractual requirements are mandated by Texas law or by administrative rules. Although applicants need not demonstrate the ability to comply with these contractual requirements at the time the application is submitted, applicants should make themselves aware of these standards before submitting a grant application. Significant issues addressed by the CPRIT contract are listed in section 15 and section 16. All statutory provisions and relevant administrative rules can be found at www.cprit.texas.gov.

10. RESUBMISSION POLICY

An application previously submitted to CPRIT but not funded may be resubmitted **only upon reissuance of this RFA by CPRIT**. An application may be resubmitted **once** and must follow all resubmission guidelines. More than one resubmission is not permitted. Given the nature of this RFA and population cohort study, an application is considered a resubmission and will only be considered if the proposed project is the same project as presented in the original submission, with allowance made for revisions to respond to the previous critique. A change in the identity of the PI for a project or a change of title of the project that was previously submitted to CPRIT or omission or modification of an aim does not constitute a new application; the application would be considered a resubmission. This policy is in effect for all applications submitted to date.

11. RENEWAL POLICY

An application funded by CPRIT under this mechanism may be submitted for a competitive renewal, **only upon reissuance of this RFA by CPRIT for the maintenance phase of the Connect study**. Competitive renewals are not subject to preliminary evaluation. Renewal applications move directly to the full peer review phase. See section 13.1.

12. RESPONDING TO THIS RFA

12.1. Application Submission Guidelines

Applications must be submitted via the CPRIT Application Receipt System (CARS) (https://CPRITGrants.org). **Only applications submitted through this portal will be considered eligible for evaluation.** The applicant is eligible solely for the grant mechanism specified by the RFA under which the grant application was submitted. The PI must create a user

account in the system to start and submit an application. Furthermore, the Application Signing Official (a person authorized to sign and submit the application for the organization) and the Grants Contract/Office of Sponsored Projects Official (the individual who will manage the grant contract if an award is made) also must create a user account in CARS. Please refer to the *Instructions for Applicants (IFA)* document for the instructions on adding Key Personnel to an application. The *IFA* document will be available when the application receipts system opens.

Applications will be accepted beginning at 7 AM central time on January 25, 2023, and must be submitted by 4 PM central time on April 18, 2023. **Submission of an application is considered an acceptance of the terms and conditions of the RFA**

12.2. Submission Deadline Extension

The submission deadline may be extended upon a showing of extenuating circumstances. A request for a deadline extension based on the need to complete multiple CPRIT or other grants applications will be denied. All requests for extension of the submission deadline must be submitted via email to the CPRIT Helpdesk within 24 hours of the submission deadline. Submission deadline extensions, including the reason for the extension, will be documented as part of the grant review process records. Please note that deadline extension requests are very rarely approved.

12.3. Scope of the Work

The goal of this RFA is to recruit health plan members from selected IHCSs into a complex, intensive, prospective cohort study led by the NCI, collect serial biospecimens and longitudinal data, and follow participants for disease outcomes, with a primary focus on cancer. The IHCS sites shall work with the NCI DCEG Coordinating Center, and others such as NORC at the University of Chicago (NORC provides the support services), and study information technology (IT) platform team, processing lab, and the NCI central repository at Frederick National Laboratory. NORC will primarily provide support for the study fieldwork activities including providing support for provision of procedures and protocols, staff training (as required) at study sites, follow-up and tracing of participants who have left the IHCS's health plan and assistance with data and specimen access. The study IT platform team has developed a tiered-access study IT platform with integrated systems for study operations, participant data collection, study research data, study research data and specimen request and approval, as well as the participant

MyConnect progressive web application. The DCEG Connect Coordinating Center also provides all Connect study communications materials and other core assets that can be customized (pending approval by the Connect Coordinating Center) for individual sites. The Connect Coordinating Center provides biospecimen collection tubes/containers and the specimen shippers.

The applicant and their institution shall furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the NCI, as needed to perform the work below. The applicant shall do the following:

1. Coordinate and integrate all of the Connect study activities including staffing decisions, prioritizing support for projects, and managing and monitoring any subcontracts.
2. Ensure quality assessment and quality control of the work performed, fostering excellent internal/external communications, tracking projects, and monitoring the budget. The applicant will report this work by preparing and submitting technical and financial reports as required by CPRIT, including quarterly enrollment reports that will be shared with the DCEG Connect Coordinating Center.
3. Coordinate training and certification for in-house study staff as required.
4. Ensure that data security and confidentiality requirements are met.
5. Work cooperatively with the NCI DCEG Coordinating Center, NORC, study IT team, and other Connect study sites in all relevant aspects of study development and execution to maximize cost effectiveness and efficiency of the study.

12.3.1. Study Planning and Preparation and Pilot Studies (6 months)

The applicant shall perform all activities necessary to prepare for participant recruitment, follow-up, and biological specimen and data collections (See Table 3). The applicant shall perform a run-in pilot phase as defined in the study protocol (IRB Protocol #000034) for recruitment and data and specimen collection to identify and resolve any barriers to successful implementation of the full study. Activities performed by the contractor include, but are not limited to the following:

- Executing planning and implementation of study protocols, including the NIH IRB protocol;
- Identifying and recruiting eligible participants;
- Collecting, processing, and shipping baseline biospecimens from consented participants;
- Electronically submitting standardized data from various data sources such as the EMR to the study IT platform;
- Using the study IT platform to manage and monitor all study activities;
- Serving as the point of contact to IHCS members and study participants to answer questions for all stages of the study;
- Working with NCI and third-party contractors to modify protocols, procedures, and study materials (if needed); and
- Performing administrative, operational, and technical duties to support productive collaboration among the study personnel at all sites, NCI, the IT study team, and the support services contractors. This shall include participation of the PI, Co-I, and/or other team members in regular calls with NCI and third-party contractors and in-study committee meetings, eg, Executive Committee (monthly), Participant Engagement Subcommittee (twice monthly), Feedback and Review Meeting (monthly), site-specific meetings (monthly), Scientific Working Groups, and RAC. In addition, this includes attending an annual in-person meeting of all stakeholders.

12.3.2. Recruitment (Years 1-5), Follow-up, and Retention (Years 6-10, pending reissue of RFA).

The applicant will perform full-scale recruitment and follow-up of participants as defined in the study protocol (see Table 3). Activities performed by the contractor include, but are not limited to the following:

- Implementing the full study with full-scale recruitment, baseline and serial specimen and data collections, and participant follow-up and retention; and
- Performing administrative, operational, and technical duties to support productive collaboration among the study personnel at all sites, NCI, the IT study team, and the support services contractors, and participating in study meetings as described above.

12.3.3. Ancillary Data and Biospecimen Collections

Activities performed by the participating site include, but are not limited to the following:

- Conducting a run-in pilot study for ancillary studies; and
- Performing administrative, operational, and technical duties to support productive collaboration among the study personnel at all sites, NCI, the IT study team, and the support services contractors, and participating in study meetings as described above.

12.3.4. Contract Closeout/Transition

The participating institution shall perform study closeout/transition activities.

12.4. Schedule of Activities

This section has been adapted from the Connect Study Protocol (#000034).

Study participant activities are expected to last through a participant's lifetime. Table 3 shows an example of a hypothetical participant's experience in the study from enrollment through active activities in the first 10 years of follow-up. The frequency of research specimens collected directly from participants, ie, blood, urine, saliva, could vary depending on age, risk of cancer, or other factors. The calendar shows retrieval of EMRs as an example of the passive activities, eg, data linkages to regional or national databases, that will be performed at regular intervals during follow-up.

Table 3. Example of Study Calendar for Data and Specimen Collections

Activities	Enrollment and Retention Activities (years)										
	Base-line	1	2	3	4	5	6	7	8	9	10
Study Eligibility Screener	X										
Enrollment	X										
Electronic Questionnaires and Personal Wearables											
Baseline questionnaire	X										
Serial assessments		X	X	X	X	X	X	X	X	X	X
Electronic Medical Records (EMR)											
EMR retrieval	X	X	X	X	X	X	X	X	X	X	X
Biological Specimens											
Blood	X			X			X			X	
Urine	X			X			X			X	
Saliva	X						X				
Tissue, precursor lesions*	X	X	X	X	X	X	X	X	X	X	X
Tissue, cancer*		X	X	X	X	X	X	X	X	X	X

* Collection of tissue from clinically diagnosed cancer precursor lesions at baseline and follow-up and cancers during follow-up, if diagnosed (see Protocol #000034 Section 7.3 *Biospecimen Evaluations*)

12.5. Application Components

Applicants are advised to follow all instructions to ensure accurate and complete submission of all components of the application. Please refer to the *Instructions for Applicants*(IFA) for details that will be available when the application receipt system opens. Submissions that are missing 1 or more components or do not meet the eligibility requirements listed in section 9 will be administratively withdrawn without review.

12.5.1. Abstract and Significance (5,000 characters)

It is the responsibility of the applicant to capture CPRIT's attention primarily with the Abstract and Significance statement alone. Therefore, applicants are advised to prepare this section wisely. **Based on the Abstract and Significance statement (and the Budget and Justification and Biographical Sketches), applications that are judged to offer only modest capacity to**

develop the Texas Connect Cohort as a component of the Connect study may be excluded from further peer review (see section 13.1).

Clearly describe the IHCS's membership and patient population, by age group and race/ethnicity, and other attributes as appropriate, eg, acculturation; ability to implement study protocols; establish the necessary integrated infrastructure (including clinical informatics capabilities, EMR access, and communications to patients through the EMR or mailings, emails, and telephone calls), finalize protocols, procedures, and study materials; and hire or assign adequately trained staff in preparation for initiating recruitment into the longitudinal cohort. Describe the PI's and Co-I's (if applicable) expertise and experience with population-based studies, including studies involving underrepresented populations. Describe the institutional commitment and sustainability plan.

12.5.2. Layperson's Summary (2,000 characters)

Provide a layperson's summary of the proposed work. Describe, in simple, nontechnical terms, the overall goals of the proposed work, the potential significance of the results to the population of Texas and the United States, and the impact of the inclusion of the IHCS's membership in the Connect study on advancing the field of cancer epidemiology early detection and prevention. The information provided in this summary will be made publicly available by CPRIT, particularly if the application is recommended for funding. Do not include any proprietary information in the layperson's summary. The layperson's summary will also be used by advocate reviewers (section 13.1) in evaluating the significance and impact of the proposed work.

12.5.3. Goals and Objectives

List specific goals and objectives for each year of the project. These goals and objectives will also be used during the submission and evaluation of progress reports and assessment of project success.

12.5.4. Timeline (1 page)

Provide an outline of anticipated major milestones to be tracked. Timelines will be reviewed for reasonableness, and adherence to timelines will be a criterion for continued support of successful applications. If the application is approved for funding, this section will be included in the award

contract. Applicants are advised not to include information that they consider confidential or proprietary when preparing this section.

12.5.5. Research Plan (20 pages)

Background: Present the rationale behind the proposed project to participate in the Texas Connect Study and its parent Connect study, emphasizing the pressing problem(s), cancer burden diversity, and cancer disparities affecting the catchment area of the IHCS, and particular strengths and expertise of the health care network and research team relevant to achieving the goals of the Connect cohort to understand the etiology and natural history of cancer.

Specific Aims: Concisely state the specific aims/overall goals to be addressed by the development of the population cohort described in the application. Describe the significance, innovation, and potential impact of the overall study on the cancer burden and unique population in Texas.

Study Design and Strategy: Refer to the Connect Protocol (IRB Protocol #000034, attached to this RFA) for a full description of the study design and schedule of activities.

1. Provide a description of the study team, their expertise and experience with the development and conduct of longitudinal cohort studies and other observational studies, participant recruitment, and the collection of biological specimens and biobanking.
2. Describe the IHCS, including its network members. Provide the demographics of members within the health plan by year, for the past 5 years, by age groups (20-29, 30-39, 40-49, 50- 59, 60-69, 70+); race and ethnicity, eg, American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White; gender (male, female); and other salient demographic factors, eg, acculturation, rurality, persistent poverty, and area deprivation index. Provide the median duration of enrollment in the health care system/plan.
3. Provide total annual number of members and number of members (a) leaving health plan annually and (b) enrolling with health plan annually, for the past 5 years, by age groups (20-29, 30-39, 40-49, 50-59, 60-69, 70+), race and ethnicity (American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White), and gender (male, female).

4. Provide information on the geographic catchment area of the clinics where biospecimen collection will occur, including which clinics cover what percentage of the health plan membership. In addition, identify if all collection sites within the offeror's group have the required infrastructure for research specimen collection. Provide additional information such as routine operation information of each collection site, eg, staffing, hours of operation, current SOPs for clinical samples, and ability to store/oversee study-specific equipment/supplies.
5. Provide information on local biospecimen (blood, urine, mouthwash samples) collection processing and short-term storage capabilities as well as the ability to ship samples for centralized lab for processing and long-term storage. Provide information such as routine operation information of local processing center, eg, staffing, hours of operation, current SOPs for clinical samples (time between collection and processing, ability to store/oversee study-specific equipment/supplies, and ability to use 2D barcodes).
6. Provide information on capabilities of retrieval of archival specimens, such as premalignant and tumor tissues. Provide information on premalignant and tumor tissues, such as preservation method, eg, frozen, FFPE, general storage time (years after diagnosis until purge) and conditions (temperature, light, humidity, location) of paraffin blocks/frozen tissue and their location.
7. Provide current cancer screening recommendations implemented in the health care plan for all its members.
8. Describe organizational policies and/or guidelines on the return of incidental findings, ie, a finding concerning an individual study participant that is discovered in the course of research and has potential clinical importance. If required to return such incidental findings, describe the approach that would be implemented in this study to handle the return of results to individuals and/or healthcare providers as necessary, including administrative and cost considerations.
9. IT and EMR Capabilities: Describe the clinical informatics team's capacity to do the following:

a. To develop a participant identification protocol to identify eligible participants, eg, from the EMR, as new members become eligible.
b. To develop a data abstraction protocol for efficiently transferring data electronically from various data sources, such as EMR, at baseline and repeatedly (as defined in the final study protocol) to the study IT platform. For instance, this could be done by uploading electronic files with standardized data fields, completion of electronic case report forms, and/or Application Program Interface (API) with the study IT platform systems.
c. To establish an internal management infrastructure necessary for recruitment and follow-up including, but not limited to, the following:
    i. Sending invitations to participate, preferably electronically via email, but other cost-effective methods are encouraged when email addresses are not available.
    ii. Integrating internal systems with study IT platform for efficient data transfer.
    iii. Establishing necessary infrastructure to serve as the primary point of contact for health plan members and participants (as defined in the final study protocol). For example, establish and host a toll-free study telephone line, and provide and monitor a study email address.
    iv. Creating a process to implement electronic lab orders for research biospecimen.

10. Describe any anticipated IT-related issues that may impede progress of the study. For example, describe any restrictions on software additions to institutional computers or networks, such as software required to scan barcodes.

11. Provide 5- and 10-year estimates of the number of projected incident cancer cases (overall and by cancer site) among potentially eligible study participants (member at least 1 year, cancer free) by age groups (20-29, 30-39, 40-49, 50-59, 60-69, 70+), race and ethnicity (American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White), and gender (male, female).

12. Provide number of known and potential cancer precursors by age, gender, and race as specified above. For example, provide definitions of precursors such as ICD codes and

procedures (codes) and treatments associated with each precursor diagnosis from the past 5 and 10 years.

13. Describe ability to perform administrative, operational, and technical duties to support productive collaboration among the study personnel at all Connect study sites, NCI DCEG Connect Coordinating Center, the study IT platform team and NORC. This will include participation in monthly Executive Committee meetings (site PIs, DCEG senior investigators); monthly meetings of the DCEG Coordinating Center with each Connect site; and monthly meetings related to data and biospecimen access for the RAC, as well as additional monthly meetings involving Study Managers, Participant Engagement Management Meetings involving 1 to 2 representatives from each site, and Feedback and Review Meetings involving the technical staff and programmers. Study responsibilities also include attending an in-person annual meeting of all participating sites and stakeholders (the next meeting anticipated to occur in October 2023 is currently being planned by the DCEG Coordinating Center). Finally, study site PIs may be asked to participate in ad hoc Working Groups charged with developing enhancements to the study design, eg, new questionnaires or new SOPs.
14. Provide a summary of institutional IRB policies and ability to establish and maintain a reliance agreement with internal IRB to cede to the NIH IRB.
15. Describe the institutional commitment and plan for sustainability.

12.5.6. Human Subjects (3 pages)

Provide a detailed plan for recruitment of subjects and/or the acquisition of samples that will meet the time constraints of this award mechanism, using the NIH PHS398 Targeted/Planned Enrollment Form. Certification of approval of these plans by the institutional IRB will be required before funding can occur.

12.5.7. Publications/References

Provide a concise and relevant list of publications/references cited for the application.

12.5.8. Budget and Justification

Provide a compelling and detailed justification of the budget for the entire proposed period of support, including salaries and benefits, supplies, equipment, participant costs, and other expenses. Based on expenses incurred at the existing Connect participating sites during the Set-up and Pilot Phase, a sample budget worksheet is provided for estimating costs for the Set-up/Pilot Phase (Year 1, Months 1-6), Recruitment Phase (Year 1, Months 7-12), and Recruitment Phase (Years 2-5) Refer to the sample budget worksheet document located in *Current Funding Opportunities* for Academic Research in CARS.

Applicants are advised not to interpret the maximum allowable request under this award as a suggestion that they should expand their anticipated budget to this level. Reasonable budgets clearly work in favor of the applicant. However, if there is a highly specific and defensible need to request more than the maximum amount in any year(s) of the proposed budget, include a special and clearly labeled section in the budget justification that explains the request. Poorly justified requests of this type will likely have a negative impact on the overall evaluation of the application.

In preparing the requested budget, applicants should be aware of the following:

- Equipment purchases allowable under the Connect RFA that are exempt from CPRIT's traditional acquisition cost cap of $5,000 include centrifuge(s) and carts. Other necessary items, such as a refrigerator, a freezer, iPads and laptop, although likely to fall below the acquisition cost of $5,000, are also exempt from this cap.
- Texas law limits the amount of grant funds that may be spent on indirect costs to no more than 5% of the total award amount (5.263% of the direct costs). Guidance regarding indirect cost recovery can be found in CPRIT's Administrative Rules, which are available at www.cprit.texas.gov. So-called grants management and facilities fees, eg, sponsored programs fees; grants and contracts fees; electricity, gas, and water; and custodial fees and maintenance fees may not be requested. Applications that include such budgetary items will be rejected administratively and returned without review.
- The maximum annual salary (also referred to as direct salary or institutional base salary) that an individual may request under a CPRIT award for FY 2023 is $200,000; CPRIT FY 2023 is from September 1, 2022, through August 31, 2023. Salary does not include

fringe benefits and/or facilities and administrative costs, also referred to as indirect costs. An individual's institutional base salary is the annual compensation that the applicant organization pays for an individual's appointment, whether that individual's time is spent on research, teaching, patient care, or other activities. Base salary excludes any income that an individual may be permitted to earn outside of his or her duties to the applicant organization.

12.5.9. Biographical Sketches (5 pages each)

Applicants should provide a biographical sketch that describes their education and training, professional experience, awards and honors, and publications relevant to cancer research. A biographical sketch must be provided for the PI and, if applicable, any additional Co-I as required by the online application receipt system. Up to 2 additional biographical sketches for key personnel may be provided. Each biographical sketch must not exceed 5 pages. The NIH biosketch format is appropriate.

12.5.10. Current and Pending Support

Describe the funding source and duration of all current and pending support for all personnel who have included a biographical sketch with the application. For each award, provide the title, a 2-line summary of the goal of the project, and, if relevant, a statement of overlap with the current application. At a minimum, current and pending support of the PI and, if applicable, the Co-I must be provided. Refer to the sample current and pending support document located in *Current Funding Opportunities* for Academic Research in CARS.

12.5.11. Institutional/Collaborator Support and/or Other Certification (4 pages)

Applicants may provide letters of institutional support, collaborator support, and/or other certification documentation relevant to the proposed project. A maximum of 4 pages may be provided.

Applications that are missing 1 or more of these components; exceed the specified page, word, or budget limits; or that do not meet the eligibility requirements listed above will be administratively rejected without review.

12.6. Formatting Instructions

Formatting guidelines for all submitted CPRIT applications are as follows:

- **Language:** English.
- **Document Format:** PDF only.
- **Font Type/Size:** Arial (11 point), Calibri (11 point), or Times New Roman (12 point).
- **Line Spacing:** Single.
- **Page Size:** 8.5 x 11 inches.
- **Margins:** 0.75 inch, all directions.
- **Color and High-Resolution Images:** Images, graphs, figures, and other illustrations must be submitted as part of the appropriate submitted document. Applicants should include text to explain illustrations that may be difficult to interpret when printed in black and white.
- **Scanning Resolution:** Images and figures must be of lowest reasonable resolution that permits clarity and readability. Unnecessarily large files will NOT be accepted, especially those that include only text.
- **References:** Applicants should use a citation style that includes the full name of the article and that lists at least the first 3 authors. Official journal abbreviations may be used. An example is included below; however, other citation styles meeting these parameters are also acceptable as long as the journal information is stated. Include URLs of publications referenced in the application.

  Smith, P.T., Doe, J., White, J.M., et al (2006). Elaborating on a novel mechanism for cancer progression. *Journal of Cancer Research*, 135: 45-67.
- **Internet URLs:** Applicants are encouraged to provide the URLs of publications referenced in the application; however, applicants should not include URLs directing reviewers to websites containing additional information about the proposed research.
- **Headers and Footers:** These should not be used unless they are part of a provided template. Page numbers may be included in the footer (see following point).
- **Page Numbering:** Pages should be numbered at the bottom right corner of each page.
- All attachments that require signatures must be filled out, printed, signed, scanned, and then uploaded in PDF format.

13. APPLICATION REVIEW

13.1. Full Peer Review

Applications will undergo review using a 2-stage peer review process: (1) Full peer review and (2) prioritization of grant applications by the CPRIT Scientific Review Council. In the first stage, applications will be evaluated by an independent peer review panel consisting of scientific experts as well as advocate reviewers using the criteria listed in section 13.3. In the second stage, applications judged to be most meritorious by the peer review panels will be evaluated and recommended for funding by the CPRIT Scientific Review Council based on comparisons of all applications and programmatic priorities. Applications approved by the Scientific Review Council will be forwarded to the CPRIT Program Integration Committee (PIC) for review. The PIC will consider factors including program priorities set by the Oversight Committee, portfolio balance across programs, and available funding. The CPRIT Oversight Committee will vote to approve each grant award recommendation made by the PIC. The grant award recommendations will be presented at an open meeting of the Oversight Committee and must be approved by two-thirds of the Oversight Committee members present and eligible to vote. The review process is described more fully in CPRIT's Administrative Rules, chapter 703, sections 703.6 to 703.8.

13.2. Confidentiality of Review

Each stage of application review is conducted confidentially, and all CPRIT Scientific Peer Review Panel members, Scientific Review Council members, PIC members, CPRIT employees, and Oversight Committee members with access to grant application information are required to sign nondisclosure statements regarding the contents of the applications. All technological and scientific information included in the application is protected from public disclosure pursuant to Health and Safety Code §102.262(b).

Individuals directly involved with the review process operate under strict conflict-of-interest prohibitions. All CPRIT Scientific Peer Review Panel members and Scientific Review Council members are non-Texas residents.

The peer review panel members for the Texas Connect for Cancer Prevention study applications will be listed on CPRIT's website.

By submitting a grant application, the applicant agrees and understands that the only basis for reconsideration of a grant application is limited to an undisclosed conflict of interest as set forth in CPRIT's Administrative Rules (Texas Administrative Code RULE §703.9).

Communication regarding the substance of a pending application is prohibited between the grant applicant (or someone on the grant applicant's behalf) and the following individuals: an Oversight Committee Member, a PIC Member, a Scientific Review Panel member, or a Scientific Review Council member. Applicants should note that the CPRIT PIC comprises the CPRIT Chief Executive Officer, the Chief Scientific Officer, the Chief Prevention Officer, the Chief Product Development Research Officer, and the Commissioner of State Health Services.

The prohibition on communication begins on the first day that grant applications for the particular grant mechanism are accepted by CPRIT and extends until the grant applicant receives notice regarding a final decision on the grant application. The prohibition on communication does not apply to the time period when preapplications or letters of interest are accepted. Intentional, serious, or frequent violations of this rule may result in the disqualification of the grant application from further consideration for a grant award.

13.3. Review Criteria

Full peer review of applications will be based on primary scored criteria and secondary unscored criteria, listed below. Review committees will evaluate and score each primary criterion and subsequently assign a global score that reflects an overall assessment of the application. **The overall assessment will not be an average of the scores of individual criteria; rather, it will reflect the reviewers' overall impression of the application. Evaluation of the scientific merit of each application is within the sole discretion of the peer reviewers.**

13.3.1. Primary Criteria

Primary criteria will evaluate the technical approach and merit, PI/research team past performance and experience, and cost effectiveness. Concerns with any of these criteria potentially indicate a major flaw in the significance and/or design of the proposed study. Primary criteria include the following:

Technical Approach and Merit:

Population: Does the application document that the health system has coordinated and integrated care provision, ie, all individual health care data (including, but not limited to, outpatient care, in-patient care, pharmacy, specialist car, and emergency care health records) are captured in the patient's EMR and can be accessed electronically by the system? If any services are not covered/captured in the EMR, details of these should be documented. Does the application provide estimates of the number of potentially eligible study participants (member of their care network for at least 1 year, cancer free) by age groups (20-29, 30-39, 40-49, 50-59, 60-69, 70+), race and ethnicity (eg, American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or Other Pacific Islander, White), and gender (male, female)?

Scope of the Work: Does the application demonstrate a clear understanding of the scope of the work, ie, study preparation, pilot phase, recruitment and follow-up, serial data and biological specimen collection, processing, and shipment, EMR data abstracting, and ability to perform this work within their IHCS infrastructure required to meet the study goals? Do they demonstrate the ability to implement study protocols and procedures as described in the study protocol, eg, linkage to the cancer registry? Does the proposal demonstrate their ability within existing infrastructure to perform data abstraction from the EMR for research purposes, and describe a plan for electronic submission of EMR data to the Connect study IT platform? Does the application describe a recruitment plan and schedule commensurate with the requirements of the study protocol?

Biological Specimens: Does the applicant demonstrate the ability to implement, comply with, and monitor study-specific protocols, including the ability to schedule and place an order for research biospecimen collection and communicate with participants who did not come in for research blood donation? Does the application document the ability of the research blood collection site, in particular the ability to accommodate walk-in visits for study biospecimen collections; perform biospecimen collection based on standing research order; track and store study-specific equipment and supplies, eg, specific blood tubes; trigger study platform at time of collection to administer a short questionnaire; and notify processing sites of incoming specimens? Does the application demonstrate the ability to collect biological tissue?

Other: Does the application demonstrate an adequate approach to quality control, quality assurance, and the process for review of task performance to optimize delivery of the task within schedule and budget and to minimize performance risk factors?

Past Performance and Experience:

Applicant Investigator and Key Personnel: Has the PI demonstrated leadership and experience in performing work of similar size (relative to the health care system's population) and/or complexity as well as qualifications? Has the PI and key personnel budgeted the required level of effort (percent effort) to this project? Does the proposal demonstrate an appropriate mix of disciplines at the optimal staffing levels needed for efficient, timely delivery of high-quality service for core and ancillary activities? Do the key personnel have appropriate experience and capabilities? Note that key personnel may include PI, Co-I, Project Manager, Research Assistant, Programmer, Study Manager, and Lab Technician.

Organizational Experience, Resources, and Facilities: Does the health care system have the appropriate organizational structure, experience, and ability to manage and execute the requirements of the study protocol? Have they demonstrated organizational experience with projects of comparable size and scope? Have they demonstrated capacity, adequacy, suitability, and availability of secure facilities, equipment, and other resources, eg, biospecimen processing and short-term storage facilities such as blood collection clinics and freezer storage/storage space available, necessary to carry out the requirements?

Cost Effectiveness: Are the specific elements of the applicant proposed costs realistic and appropriate for the work to be performed, reflective of a clear understanding of the requirements, and consistent with the unique methods of performance and materials described in the applicant's technical proposal?

Human Subjects Evaluation: The applicant's proposal must address the involvement of human subjects and protections from research risk relating to their participation, using the standard NIH format. The application should include the NIH Targeted/Planned Enrollment Report. The reviewers will evaluate the proposal with regard to 4 issues: Risks to Human Subjects, Adequacy of Protection Against Risks, Potential Benefits of the Proposed Research to the Subjects and Others, and Importance of the Knowledge to be Gained.

Duration: Is the stated duration appropriate for the proposed work?

14. KEY DATES

RFA

RFA release	January 17, 2023

Application

Online application opens	January 25, 2023, 7 AM central time
Application due	April 18, 2023, 4 PM central time
Application review	April 2023-June 2023

Award

Award notification	August 2023
Anticipated start date	August 31, 2023

15. AWARD ADMINISTRATION

Texas law requires that CPRIT grant awards be made by contract between the applicant and CPRIT. CPRIT grant awards are made to institutions or organizations, not to individuals. Award contract negotiation and execution will commence once the CPRIT Oversight Committee has approved an application for a grant award. CPRIT may require, as a condition of receiving a grant award, that the grant recipient use CPRIT's electronic Grant Management System to exchange, execute, and verify legally binding grant contract documents and grant award reports. Such use shall be in accordance with CPRIT's electronic signature policy as set forth in chapter 701, section 701.25.

Texas law specifies several components that must be addressed by the award contract, including needed compliance and assurance documentation, budgetary review, progress and fiscal monitoring, and terms relating to revenue sharing and intellectual property rights. These contract provisions are specified in CPRIT's Administrative Rules, which are available at www.cprit.texas.gov. Applicants are advised to review CPRIT's Administrative Rules related to contractual requirements associated with CPRIT grant awards and limitations related to the use of CPRIT grant awards as set forth in chapter 703, sections 703.10, 703.12.

Prior to disbursement of grant award funds, the grant recipient organization must demonstrate that it has adopted and enforces a tobacco-free workplace policy consistent with the requirements set forth in CPRIT's Administrative Rules, chapter 703, section 703.20.

CPRIT requires award recipients to submit an annual progress report. These reports summarize the progress made toward the research goals and address plans for the upcoming year. In addition, fiscal reporting, human studies reporting, and vertebrate animal use reporting will be required as appropriate. Continuation of funding is contingent upon the timely receipt of these reports. Failure to provide timely and complete reports may waive reimbursement of grant award costs and may result in the termination of the award contract. Forms and instructions will be made available at www.cprit.texas.gov.

16. REQUIREMENT TO DEMONSTRATE AVAILABLE FUNDS

Texas law requires that prior to disbursement of CPRIT grant funds, the award recipient must demonstrate that it has an amount of funds equal to one-half of the CPRIT funding dedicated to the research that is the subject of the award. A grant recipient that is a public or private institution of higher education, as defined by §61.003, Texas Education Code, may credit toward the grant recipient's matching funds obligation the dollar amount equivalent to the difference between the indirect cost rate authorized by the federal government for research grants awarded to the grant recipient and the 5% indirect cost limit imposed by §102.203(c), Texas Health and Safety Code. Grant applicants are advised to consult CPRIT's Administrative Rules, chapter 703, section 703.11, for specific requirements regarding demonstration of available funding. The demonstration of available matching funds must be made at the time the award contract is executed, and annually thereafter, not when the application is submitted.

17. CONTACT INFORMATION

17.1. Helpdesk

Helpdesk support is available for questions regarding user registration and online submission of applications. Queries submitted via email will be answered within 1 business day. Helpdesk staff are not in a position to answer questions regarding scientific aspects of applications.

Hours of operation: Monday through Friday, 8 AM to 6 PM central time

Tel: 866-941-7146

Email: Help@CPRITGrants.org

17.2. Scientific and Programmatic Questions

Questions regarding the CPRIT program, including questions regarding this or any other funding opportunity, should be directed to the CPRIT Director of Academic Research.

Tel: 512-305-8491

Email: research@cprit.texas.gov

Website: www.cprit.texas.gov